RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

Vol. 48 APRIL 1947 No. 4

Reasons for the Common Anatomic Location of Pulmonary Tuberculosis[1]

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THE EARLY pathologists recognized that the principal lesions of pulmonary tuberculosis in European adults were cavitations and fibrocaseous nodules in the cephalad third of the lungs, and it was realized that the first cavities usually appeared near the apex, more often on the right. Precise knowledge of the development of all types of pulmonary disease was made possible by the roentgen ray, which confirmed and refined earlier views and established the frequency of healed primary complexes in the lungs and thoracic lymph nodes. The studies of Sweany (1) on location of single cavities may be taken as one of the best quantitative reports, fully confirming the right-sided and juxta-apical predilection of progressive lesions in adults.

The work of Medlar proved that in cattle and in rabbits the progressive lesions were usually far more numerous at the opposite anatomical site, namely the juxta-diaphragmatic and dorsal regions (2, 3). Medlar also observed, however, that in rabbits which had been kept erect by a harness for eleven hours each day the localization resembled that in man (3). It thus became evident that in animals with some resistance to tuberculosis the disease may become arrested in the parts of the lungs which are on a level with the heart, in the gravitational field, while progressing in those parts which are farthest above the heart. In animals moving on four feet, progress occurs in the dorsal part of the lower lobe, but in those which are erect, even for half of the day, progressive lesions are extremely rare at the base and are frequent in the apical third of the lung.

Older theories, which attributed apical localization in man to the relative coldness of the apex, or to the peculiarities of the bronchi, are out of harmony with these animal observations, which prove that the explanation must lie in the effect of the gravitational field on the resistance in various parts of the lung. Röder's theory (4) that increase in hydrostatic pressure raised the vitality of cells, and thus made basal cells more resistant than apical ones, is nullified by two facts. In the air-filled lungs, pressure on all extravascular cells is uniform throughout the whole organ, and the disease flourishes in the extravascular tissues. If lowering pressure on the cells lowered resistance to tuberculosis, the disease would be more rapidly progressive as barometric pressure was reduced, but actually the beneficial effects of higher altitudes on human

[1] Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1–6, 1946.

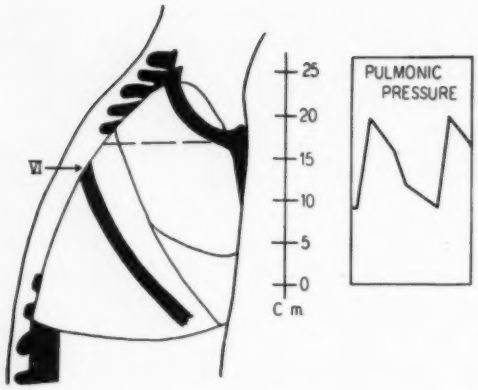

Fig. 1. The pressure curve in the pulmonary artery during one heart cycle is shown, in centimeters of water, and the lateral profile of the right lung, with height in centimeters above the center of mass of the right ventricle. The vertebrae and first and sixth ribs are indicated and the dotted line shows the level at which pulmonary flow must cease because hydrostatic pressure exceeds pulmonic arterial pressure. In mitral stenosis, the arterial pressure is two to six times as high as in this normal subject, apical ischemia does not occur, and apical tuberculosis is rare.

tuberculosis are generally conceded, and confirmed by animal experiment (5). Thus it was that Pinner and Rich, in their recent books on phthisis, stated that the cause of apical localization of adult type tuberculosis is unexplained.

The work of Cournand and Richards (6) has shown that, when recumbent, men have a systolic pulmonary arterial pressure of 18 to 30 mm. Hg. As the cardiac output is less when the subject is sitting or standing than in recumbency, and pulmonary arterial pressure varies with the output, even lower pressures must occur in the right ventricles of persons who sit or move but little while on their feet. This means that the column of blood from the right heart to the apical part of the lungs exerts an equal or greater pressure (Fig. 1). In view of the fall of pressure along the course of a vessel, there can scarcely be any blood flow, and no formation of lymph or tissue fluid, at the upper third of the lungs under these conditions. Because of the length and tortuosity of the right pulmonary artery, pressure on that side will be lower and the bloodless region larger than on the left. In the horse (7), with a pulmonary arterial pressure of 35 to 58 mm. Hg, and presumably also in cattle, the dorsal part of the lungs must be equally bloodless while the animal is at rest. There are no data on rabbits in the postures studied by Medlar and Sasano (2), but values for pulmonic pressure as low as 6 mm. Hg have been recorded in the laboratory (7), and it seems probable that even in these small mammals the effect of gravity on the pulmonary blood column may greatly reduce the formation of lymph and flow of blood in the regions farthest above the heart.

As is well known, primary lung lesions initiated prior to development of resistance are disseminated generally throughout the lungs of men, cattle, and rabbits. It seems probable that in animals or men with reinfection or with rapid development of high resistance, an inadequate pulmonary blood flow, for many hours each day, may permit tuberculosis to progress in the lung field highest above the heart, while lower parts enjoy a considerable degree of immunity. In adults, progressive lesions observed soon after reversal of a negative skin test are usually in the upper lung field, and in the usual instances of "reinfection," apical disease progresses and the opposite apex becomes involved even though other regions, in spite of a constantly positive sputum, remain free for months, years, or decades.

Alveoli which are aerated through the bronchi, but deprived of the normal flow of pulmonary arterial blood, with its low oxygen saturation, will have the highest oxygen and lowest carbon dioxide content. This favors the growth of tubercle bacilli (5). It is obvious that in the bloodless zone toxins will accumulate, while in other regions they will be diluted and carried away by blood and lymph. Lymph also will remove bacilli to regional nodes, where their destruction leads to new formation of antibodies. In the ischemic zone, the antibody level will be low, for the quantity of antibody and the number of phagocytes brought by the blood will be negligible. Only during activity or recumbency,

both of which raise pulmonic pressure, will the blood flow in the apical regions equal that in other parts of the lungs and restore to the apex its full measure of resistance. In rabbits, eleven hours of erect posture out of twenty-four reversed the location of progressive lesions. In man, apical disease is particularly common in sedentary persons and in those who get few hours of sleep.

A comparison of the known pulmonic pressures with the anatomical and gravitational effects on flow to the regions commonly the site of progressive lesions suggests but does not prove that flow to these regions actually is diminished. Tests of a conclusive nature can be made by intravenous injection of small quantities of radioactive isotopes having soft gamma radiation. With suitable detecting devices, the number of impulses from various pulmonary fields can be registered immediately after an injection, when the material is passing through the lungs, and the effects of the recumbent and erect postures on the relative number of impulses at apex and base can be compared. Until such data are obtained, the reduced or arrested flow in the superior parts of the lung and the actual amount of lung so affected on each side are purely speculative.

One reason for accepting the probability that relative ischemia is the basis for the apical localization of phthisis in man is the very low incidence of progressive apical lesions in patients with mitral stenosis, and the very high incidence in those with pulmonic stenosis. In the former, pulmonic arterial pressure may be as high as 116 mm. Hg and usually is over 40 mm. (6); in the latter group pulmonic pressure and flow must be lower than in normals. In pulmonic stenosis, the apical regions probably are bloodless even at the peak of the patient's physical activity, and not merely when he is standing quiet. At all times the proportion of poorly perfused lung is far greater than in normal subjects. Though only a few such individuals reach adult life, apical tuberculosis has been active in a notable proportion (8). In mitral stenosis, although it is particularly prevalent in the poor and leads to malnutrition, active apical tuberculosis is extremely rare (9), and comparison of the force of gravity with the level of pulmonic pressure makes it improbable that apical ischemia can occur in most of these patients. In the absence of data on blood flow in the normal apex in the recumbent and erect position, this statistical material is the most convincing support of the theory that the erect posture robs the apical zone of the blood and lymph flow, and hence of much of the protection enjoyed by other parts of the lungs in those who have developed resistance to tuberculosis.

The significance of this theory, in treatment by bed rest and collapse, has been presented elsewhere (10). At this time, it is merely necessary to stress that absolute recumbency, not rest in the propped up or sitting posture, is the factor most important in management. Perhaps even short periods of recumbency, at intervals of a few hours, can lower toxin concentration and turn the delicate balance against progress of the apical lesion. In any event, getting out of bed for short periods, to eat or to use toilet facilities, probably has no deleterious effect on the lesions, while improving the patient's morale and appetite. Granting that rest in the open air may help to keep patients quiet and recumbent, it can be argued that recovery does not depend on the rural atmosphere, or even on the lakes, woods, and mountains which, though dear to men like Trudeau, are hateful to many urban citizens, who long for home and friends. The wilderness sanatoria seem especially depressing to women, who echo Tibullus' query: "*Dulcius urbe quid est? An villa sit apta puellae?*"

The arrest of pulmonary tubercu'osis still depends on aiding the patient's own powers of resistance rather than on antibiotics. If his morale and resistance are raised by moving him into a new environment, sanatorium treatment will be helpful, but it seems clear that the really ef-

fective agent—rest flat in bed—requires no special apparatus or nursing, and is not dependent for its success on the absence of city sights and sounds. In 1882 Ewart closed his Gulstonian lectures (11) on pulmonary tuberculosis with a remark which is equally valid today: "The treatment of pulmonary cavities may look forward to a better future, if it seeks its foundation in a sound pathology."

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The Roentgen Findings in Early Coccidioidomycosis[1]

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IT SEEMS VERY probable that the next few years will see a decided increase in the number of sporadic cases of coccidioidal infections reported from various sections of the United States where it is not now endemic. The unsettled socio-economic conditions of the post-war world with its accelerated rate of population migration, the anticipated increase in vacation travel to or through endemic areas, and the increasing use of the airplane and other rapid means of long distance transportation, all point to such a conclusion.

It has repeatedly been shown that coccidioidomycosis may be acquired by no more exposure than that incidental to passing through an area of endemic infection. These areas include large sections of the arid Southwest, having in common long, hot, dry and dusty summers. A definite correlation has been established between the number and severity of dust storms and the incidence of coccidioidal infections in these regions (4). Newly arrived residents have been observed to be particularly susceptible to the disease. The known zones of infection are especially the great central valley of California (the San Joaquin), the whole of Arizona (but particularly the regions about Phoenix and Tucson), Southwest Nevada, and parts of New Mexico and Western Texas. The disease is acquired by inhalation of dust contaminated with chlamydospores of the fungus, *Coccidioides immitis*. It is presumed that the fungus grows in the soil or on vegetation in the rainy season and that the spores dry up, break off, and are scattered by the wind in the dry season. An important intermediary host may be small rodents, which have been found to show a high incidence of nodular coccidioidal lung foci (13). The incubation period averages about ten days to two weeks, sufficient time for travel, under modern conditions, from an endemic zone to any part of the country.

HISTORY

For the purpose of this paper, the following summary of the history of coccidioidomycosis is sufficient. Beginning with the discovery of the disease in its relatively rare disseminated form in Argentina in 1892 and in California in 1894, and the identification of the organism in 1904, there accumulated, over many years, detailed information concerning the behavior of the condition in its malignant variants.

In 1935 a primary, usually spontaneously recovering, pulmonary onset was proved, having far wider incidence than the serious disseminated form (14). There followed immunological proof of a still broader subclinical involvement as evidenced by the large proportion of residents of endemic areas who were shown to react positively to coccidioidin skin tests (26).

Throughout, the clarification of the roentgen manifestations of the disease naturally lagged behind that of clinical, pathological, and immunological considerations, inasmuch as the pioneering investigators were not radiologists. Before the war there were, in addition to the roentgenologic data given in articles not primarily roentgenologic, a number of papers dealing specifically with the roentgen manifestations (Powers, 25; Carter, 3; Winn and Johnson, 34). But these were generally based on cases either few in number or without adequate serial studies.

One of us (Carter), in 1941 (3), attempted such a study, stating that detailed roentgen characterization of the primary pulmonary disease must await serial roent-

[1] From the University of Southern California. Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1–6, 1946.

gen observations in many cases continued well past the period of clinical illness. These requirements have been met due to the circumstance that a number of endemic areas were especially favorable for military training. The hazard was known. Precautions were taken with the able advice and assistance of C. E. Smith. Capable clinicians and radiologists were available; these were alerted and adequate hospital and follow-up observations were made, accompanied by thorough immunological, laboratory, and roentgenologic studies. Detailed residence and travel records were obtained in each case. As a result, hundreds of cases have been thoroughly studied roentgenologically, with all associated information needed, in a manner not practicable in civilian life. A number of radiologists have each seen a large series of cases, up to a hundred or more (5, 10, 15, 18, 22, 23, 27, 29, 32). This overcomes the irregularity of sampling in fewer cases, gives adequate display of less frequent manifestations, and permits correlation of varied points of view of individual authors.

Some differences of opinion are evident, particularly in the earlier papers. These may be explained in part by different concepts of pathogenesis or simply by differences in the descriptive terms used, but perhaps more important are the varying concepts derived from differences of sampling in cases seen. One of us (3), for example, had encountered an exceptional number of the disseminated infections but relatively few of the early cases, and these were, on the average, relatively severe. His experience, moreover, was dominated somewhat by the fact that in a charity hospital adjacent to, but not in, a major endemic area, the initial infection and illness were apt to arise elsewhere and not be seen by him unless the attack were prolonged or of over-average severity. Also, among his patients there was a predominance of the colored and dark-skinned races, who are prone to coccidioidal infections of unusual severity. Correspondingly, mediastinal adenopathy was stressed in his presentation (1941) of primary coccidioidomycosis to an extent not supported by other authors. Colburn (5), reporting on an "epidemic," speaks only of hilar thickening and enlarged hilar nodes, and not at all of mediastinal adenopathy. His cases, numbering 75, would appear to be of average sampling, weighted neither by an excess of cases milder or more severe than average.

DIAGNOSIS

The clinician working in endemic areas and accustomed to seeing many cases of "valley fever" has little difficulty in recognizing the disease. The diagnosis is relatively simple once the condition is thought of, but recognition of the sporadic case which appears in a non-endemic area requires special alertness on the part of the physician to the possibility of such an infection. The diagnosis of coccidioidomycosis should be considered in the case of any person who, having recently returned from a zone of endemic infection, presents evidence of a respiratory disease. An intradermal coccidioidin skin test with a 1/100 concentration of potent extract, if negative, will generally rule out the disease in all but a few of the more severe disseminated infections (10, 31). If the test is positive, under these circumstances, a presumptive diagnosis of coccidioidomycosis is warranted. The diagnosis is established with certainty by positive precipitin or complement-fixation tests, which are found only in the presence of active infection. These tests are unfortunately open to the objection that some of the milder cases may give a negative reaction. Final proof is obtained by culture of sputum or guinea-pig inoculation, with demonstration of the causative organism.

Clinically, the conditions which are most likely to be confused with acute primary coccidioidomycosis are influenza and primary atypical pneumonia (19). The patient complains of backache, headache, or general aching, or marked weakness, slightly sore throat, loss of appetite, and various indefinite gastro-intestinal disturbances. Cough is nearly always present and

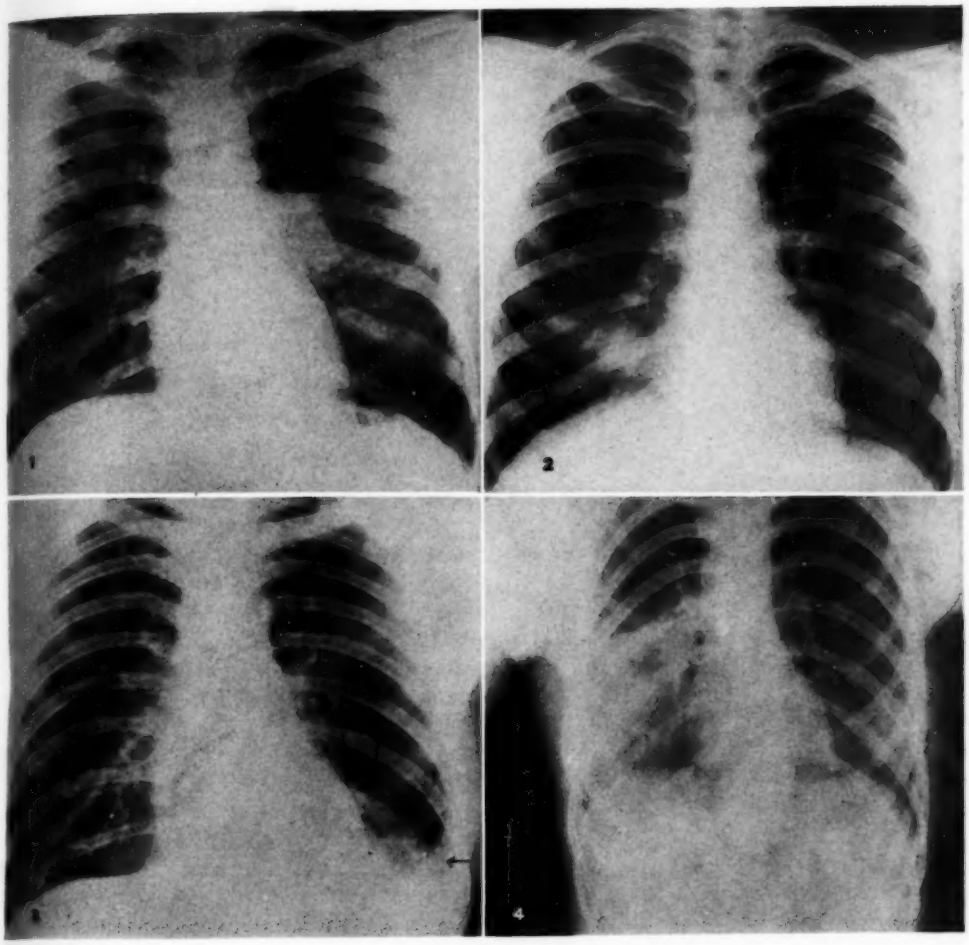

Fig. 1. Acute primary coccidioidomycosis. Left hilar thickening.

Fig. 2. Acute primary coccidioidomycosis. Local zone of pneumonitis in the medio-basal portion of the right lung.

Fig. 3. Acute primary coccidioidomycosis. Small amount of infiltration at the left base, associated with slight pleural effusion.

Fig. 4. Acute primary coccidioidomycosis. Extensive pneumonitis in the right lower lung. Two weeks later the lung had cleared.

is usually of a dry, irritating type, though small amounts of sputum may be raised. The temperature is of a spiking type, usually to 100–102° F. The white blood cell count is usually elevated, averaging 10,000 to 12,000, with mild increase in the neutrophil percentage. Eosinophilia of 3 to 15 per cent is frequently encountered and, when present, is a helpful diagnostic sign. One striking feature which is of especial importance in differentiating coccidioidomycosis from the commoner respiratory conditions is the occurrence of chest pain in a very high percentage of patients (87 per cent of acute cases) (18). This varies in degree from a sense of substernal tightness or constriction to a very sharp knife-like pain of pleural type.

Usually after three to ten days the temperature falls to normal, and the patient feels that he has recovered from his illness, even though films taken at this time

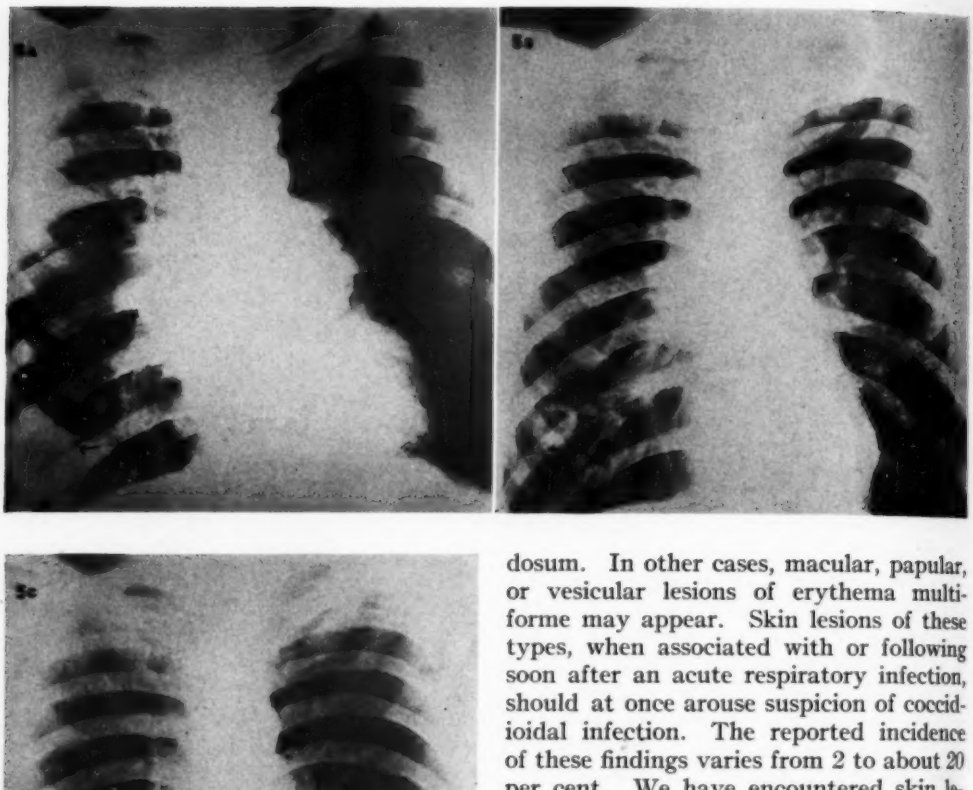

Fig. 5. A. Acute primary coccidioidomycosis. An unusually severe case with hilar and mediastinal adenopathy. Local zone of infiltration at right base. B. Primary coccidioidomycosis. The mediastinal and hilar adenopathy shown in A has regressed after a period of six weeks; the local zone of pneumonitis at the right base has been replaced by an isolated ring-like cavity. C. The mediastinal and hilar lymphadenopathy shown in B has further regressed after a period of ten weeks; the cavity previously present has disappeared, leaving a residual nodule.

may show considerable residual infiltration. Then, one or two weeks later, painful nodules may develop on the shins and elsewhere, characteristic of erythema nodosum. In other cases, macular, papular, or vesicular lesions of erythema multiforme may appear. Skin lesions of these types, when associated with or following soon after an acute respiratory infection, should at once arouse suspicion of coccidioidal infection. The reported incidence of these findings varies from 2 to about 20 per cent. We have encountered skin lesions in about one of every seven cases of acute infection. Acute arthritis and conjunctivitis are often associated with these allergic skin manifestations. The joints become quite tender and painful but usually not so swollen as in rheumatic fever, and the response to large doses of salicylates is not nearly so prompt or striking.

ROENTGEN FINDINGS IN ACUTE PRIMARY COCCIDIOIDOMYCOSIS

In the earlier stages of initial infection the roentgen findings are quite non-specific and could as well be explained by ordinary bronchopneumonia, primary atypical pneumonia, rheumatic pneumonitis, or, if the upper lung fields are selectively involved, by tuberculosis. Only special alertness to the possibility of the disease would cause it to be considered.

A film of the chest taken at the time of onset will show some degree of pulmonary

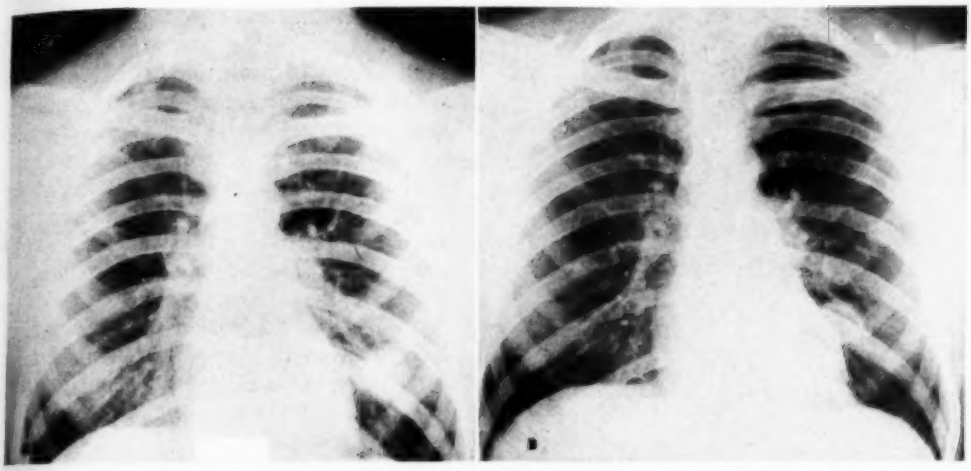

Fig. 6. Primary coccidioidomycosis. A. Nodular, well circumscribed lesion in the lower left lung. B. In the nodular lesion shown in A central cavitation is developing after a period of six months.

infiltration in about nine out of ten cases. Infiltrations vary in extent from the slightest fuzzy thickening of hilar shadows to extensive consolidations occupying a major portion of a lung field. The infiltrations are mostly unilateral, homogeneous, usually hilar or basal in location, and show little tendency to lobar distribution. They vary in density from the lightest veil-like haze to consolidations approaching, but rarely equaling, the opacity of lobar pneumonia. As a rule, they are more uniform, less patchy, more circumscribed than the usual bacterial bronchopneumonias.

To the radiologist, the appearance is most likely to suggest the findings encountered in primary atypical pneumonia. And, as a matter of fact, it is not often possible, on the basis of roentgenograms alone, to differentiate the two conditions (19). To add to the confusion, the clinical signs and symptoms of the two diseases are often quite similar. Differentiation may be possible only by resort to coccidioidin or specific laboratory tests. Indeed, it would seem advisable in endemic zones to do routine skin tests on all persons suspected of primary atypical pneumonia

The similarity between acute coccidioidomycosis and primary atypical pneumonia may be carried further to include rheumatic pneumonitis. That the whole picture of acute coccidioidomycosis may closely resemble rheumatic fever is shown by the fact that "desert rheumatism" is one name for the mycosis, and the fact (Griffith, personal communication) that in military service, where alertness to the disease is high, a number of cases were transferred to centers where rheumatic fever was treated, there to be proved coccidioidomycosis. While the primary event in rheumatic pneumonitis is the occurrence of an anaphylactic angiitis with multiple local infarctions, the presenting evidence upon the roentgenogram would be a highly cellular and exudative reaction in the alveoli and adjacent structures (16). As a matter of fact, all these diseases—primary atypical pneumonia, coccidioidomycosis, and rheumatic pneumonitis—are ones in which a highly cellular response to infection occurs, and it is only natural that they should reveal considerable similarity, roentgenographically. Moreover, the migratory tendency which is so pronounced a feature of rheumatic pneumonitis is also encountered to a lesser degree in primary atypical pneumonia and occasionally in coccidioidomycosis.

PERSISTENT COCCIDIOIDAL INFECTIONS

With persistence of coccidioidal infection, the patient may complain of low-grade

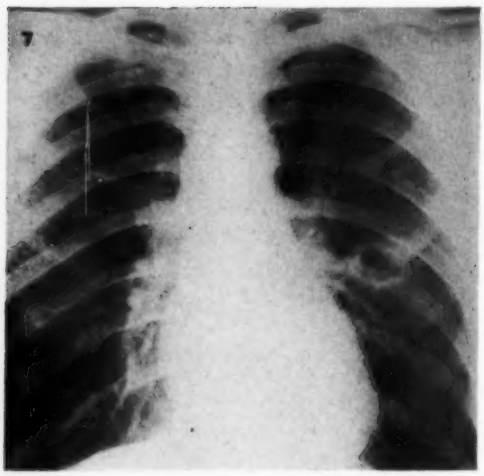

Fig. 7. Primary coccidioidomycosis. Ring-like cavity in the left midlung.

fever, weakness, abnormal fatigability, chronic cough, intermittent chest pain, and mild to moderate weight loss. Hemoptysis may occur whether or not a cavity is present. If the patient is seen at this time, a clinical diagnosis of pulmonary tuberculosis may be made. Moreover, the chest films may confirm this erroneous impression, especially if persistent pneumonitis occurs in the upper lung fields. Failure to find acid-fast bacilli in the sputum has usually been the decisive factor in stimulating search for other possible infections. Inasmuch as the great majority (85 to 90 per cent) of acute coccidioidal infections clear relatively rapidly within a matter of two to six weeks, and are usually hilar or basal in location, the ultimate differentiation from tuberculosis is only occasionally a difficult problem. Nevertheless, tuberculosis enters frequently enough into the differential diagnosis that, in cases seen in endemic areas, it would appear time-saving to make tuberculin and coccidioidin tests routinely, at the same time. Moreover, certain cases of coccidioidal pneumonitis are found to persist for many months or years before finally clearing. We have seen 21 patients with benign, non-disseminated infections of this type lasting from three months to over two years (18). Confusion with tuberculosis is especially likely in this group.

One form of protracted primary coccidioidomycosis deserves special consideration. In this, there is profuse involvement usually in an upper lobe, in which multiple cavities are evident in a zone of confluent infiltration, identical in appearance with advanced ulcerative tuberculosis, but with persistent failure to find the acid-fast bacillus. Coccidioidomycosis may be identified through recognition of the organism, by coccidioidin, or complement-fixation test. One of us (Carter) has seen several of these cases through the alertness of the Olive View Sanatorium. Complete regression may occur in a manner which is slow for coccidioidomycosis but which would be sensational for tuberculosis.

It is not yet fully evident how far the early phase of pulmonary infection by histoplasmosis may come into comparison with coccidioidomycosis. That both diseases have residual calcifications is now well established. The active phase of histoplasmosis has not yet been studied in a sufficient number of cases. Palmer (24) has shown comparable pulmonary involvement. One of his cases, at least, revealed a hilar and mediastinal adenopathy more advanced than is seen in any but the most severe of coccidioidal infections. As in coccidioidomycosis, the parenchymal lesions may be of indolent type, prone to slow resolution. The widely different endemic areas and the early age at which histoplasmosis occurs should make the need for differentiation relatively infrequent.

Torulosis, like coccidioidomycosis, is considered to have a pulmonary onset. While it is prone to be generalized, with a special predilection for the central nervous system (Hamilton and Tyler, 17), a fifth of the patients, or so, have pulmonary lesions. While these have not been typed roentgenologically with any degree of completeness, confluent lesions have been illustrated which tend to regress over periods of months even though the central nervous system involvement supervenes.

Mediastinal adenopathy accompanies

many of the more severe and protracted coccidioidal infections. Approximately one-third of the cases of persistent pneumonitis will show some degree of associated adenopathy, while practically all fatal cases will present this finding at least some time during their course. Mediastinal adenopathy, on the other hand, is uncommon in association with the usual acute transitory infections and is almost never seen with focalized infections of the nodular or cystic types, later to be described.

The occasional patient in whom mediastinal adenopathy is the dominant or sole roentgen finding may be initially believed to have Hodgkin's disease, primary tuberculosis, sarcoidosis, etc. Mediastinal adenopathy accompanied by hilar infiltration has been mistaken for bronchiogenic carcinoma. The fact that patients with mediastinal coccidioidal adenopathy are usually chronically ill, with weight loss, weakness, anorexia, and anemia, adds to the confusion with malignant neoplastic disease. The association of fever, chest pain, and perhaps eosinophilia may help in the differentiation. But even here, the clinical findings may be misleading, since chest pain is not infrequently a prominent characteristic of bronchiogenic carcinoma, and fever and eosinophilia may accompany Hodgkin's disease.

Pleural effusion is encountered in approximately one-fifth of all acute primary cases but ordinarily is so small in amount as scarcely to fill the costophrenic angle; it resolves rapidly and completely as a rule. In a small percentage of cases, pleurisy with effusion may be massive and persistent, so that in the presence of spontaneous effusions of unknown origin, the possibility of coccidioidomycosis should be considered when the patient has recently returned from a zone of endemic infection.

RESIDUAL COCCIDIOIDAL FOCI

In view of the fact that the acute primary phase of coccidioidomycosis is often mild, transitory, and not unlike the common respiratory infections, the disease is often passed off as a simple "cold" or "flu" and

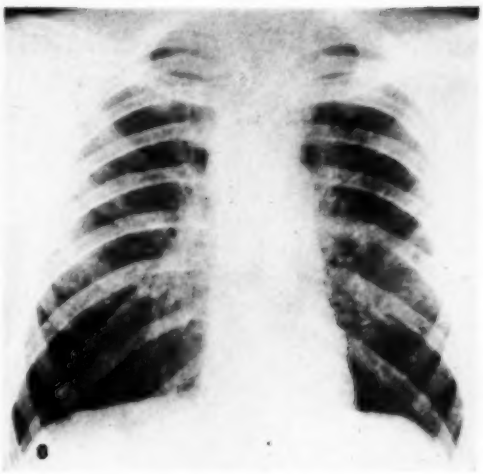

Fig. 8. Primary coccidioidomycosis. Lumpy mediastinal adenopathy. Infiltration radiating from hilar regions. Chest films were entirely normal after a period of two and one-half months.

readily forgotten. It thus not infrequently happens that the roentgenologist encounters residual "burned-out" foci of coccidioidomycosis without any apparent history of antecedent infection. This is particularly true of radiologists engaged in mass survey or routine hospital photoroentgen studies. The roentgenologist may be surprised to see a sharply circumscribed nodule 1 to 4 cm. in diameter, which he may suspect of being an uncalcified primary tuberculous focus or a solitary metastasis. In the case of multiple nodules, he is likely to make a diagnosis of extensive metastatic carcinoma, for what is actually a benign condition. At other times, isolated thin-walled ring-like cavities 1 to 8 cm. in diameter are encountered which, when they occur in the middle or lower lung fields, may readily be mistaken for congenital cysts. When apical or subapical in origin, they are often misdiagnosed as being of tuberculous origin.

The acute illness in those patients followed directly through from a preliminary stage of pneumonitis to nodule formation is usually no more severe or prolonged than in cases in which infiltrations clear completely. (An exception is the occasional case in which numerous widely scattered

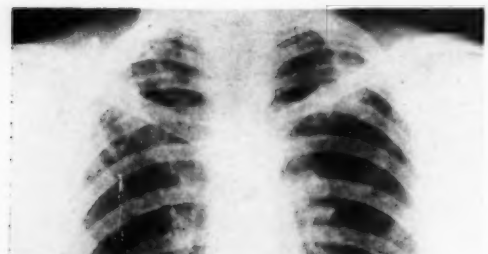

Fig. 9. Primary coccidioidomycosis. Tuberculosis-like apical infiltration with infraclavicular cavities.

patches of pneumonitis give rise to multiple nodular foci. The onset in these cases is typically quite severe.) The initial illness in cases destined to develop cavities is generally more acute, with symptoms of malaise, cough, chest pain, and fever to 100 to 103° lasting two to four weeks. Infiltrations preceding nodulation or cavitation are fairly homogeneous zones of consolidation 2 to 10 cm. in diameter, which tend to round out with decrease in size, leaving the isolated nodule or cavity at the center of the zone of previous pneumonitis. The elapsed time from the initial pneumonitis to nodule formation averages about three to six weeks but occasionally is as long as two or three months. Cavities not infrequently develop through central excavation of nodular foci over a period of several weeks or months and, when arising in this fashion, are usually smaller and thicker-walled than the cyst-like cavities which arise directly from the initial consolidation and have a more doughnut-like appearance.

All nodules and cavities have proved remarkably indolent, slow in evolution and benign in character. But minor fluctuations in cavity size and wall thickness have been recorded in practically all cases. At times, fluctuations in cavity size were of such degree and occurred so rapidly as strongly to suggest ballooning due to air trapping. Some of the larger thinner-walled cavities have been observed to collapse rapidly over a period of several days, either to reappear just as suddenly or to disappear permanently. Others have gradually diminished in size to end as small nodules. But many months are generally required for cavities to disappear completely. Of one group of 35 cavities followed for an average of seven and one-half months, less than half had disappeared in that time, and some have been followed for as long as two years without appreciable reduction in size. As for the coccidioidal nodules, these appear to persist for many years with little change. We have been able to follow only a single one of these foci through to complete resolution. From other studies (Cox and Smith, 7; Aronson, 1; Butt and Hoffman, 2), it is evident that some, at least, go on to eventual calcification.

The differentiation of these coccidioidal lesions from conditions which they simulate is based to a large extent on the marked discrepancy between the clinical and roentgen findings. The nodular and cystic foci of coccidioidomycosis are essentially benign residual foci which persist for many months or years following the initial acute disease without materially impairing the patient's health or well-being. A large percentage of these residual foci are discovered on routine roentgen examinations without prior clinical indication of disease. In one survey, 15 of 23 nodular foci and 13 of 35 cavity cases were so discovered. The patient's temperature, white blood cell count, complement-fixation titre, and sedimentation rate are usually in the normal range, and the disease apparently never spreads to other lung tissue or disseminates. Patients with residual cavities not infrequently complain of intermittent sticking chest pain and occasionally cough and hemoptysis. The absence of tubercle bacilli in the sputum on repeated examinations helps to direct attention away from tuberculosis as the source of infection.

On the other hand, *Coccidioides immitis* is, as a rule, not difficult to recover when a cavity is present and the patient is raising even a small amount of sputum.

Roentgenologically, most coccidioidal cavities are so characteristic that they are seldom confused with other conditions when occurring in endemic areas. A solitary thin-walled ring-like shadow without surrounding infiltration is typical (33). Cavities are occasionally encountered with walls so thin and sharply defined as closely to simulate congenital cysts. Sante and Hufford (28) have described annular lung shadows in certain pyogenic infections which look remarkably like those of coccidioidomycosis. We have seen three cases in which cavities contained fluid and were surrounded by infiltration in such a fashion as to suggest lung abscess. The differentiation from tuberculosis in the case of apical cavities, and especially those which are occasionally surrounded by coccidioidal pneumonitis, is often not radiographically possible. Certain other mycotic infections may produce lesions closely resembling those of coccidioidomycosis, roentgenographically. For instance, a case of geotrichosis has been illustrated (6) which displayed multiple ring-like cavities identical with those seen in coccidioidomycosis. A case of torula infection of the lung is also illustrated which closely resembles the nodular type of coccidioidal lesion (6).

DISSEMINATED COCCIDIOIDAL INFECTIONS

A discussion of disseminated coccidioidal infections is not in the scope of this paper. Suffice it to say that the patient not infrequently first presents himself for medical care with evidences of disseminated foci already present. Often a history of an acute antecedent infection cannot be obtained or is overshadowed by the severity of the disseminated disease. In white patients the presenting symptoms are frequently those of meningitis, while in the Negro the presenting evidence will more often be that of multiple cold abscesses arising subcutaneously or from caseous lymph nodes or bone foci. In these cases the roentgen findings in the chest will be primarily those of mediastinal adenopathy associated with varying degrees of infiltration up to massively confluent miliary disease with multiple areas of bone destruction resembling metastatic carcinoma. Benign chronic indolent forms of the disease are also encountered which persist for many years in the form of small warty outgrowths on the skin, chronic draining sinuses, or chronic coccidioidal osteomyelitis, without seriously impairing the patient's health or jeopardizing his life. The diagnosis is easily made by biopsy or culture from the local lesion.

SUMMARY

1. The diagnosis of coccidioidomycosis is not a difficult one if the physician is alert to the possibility of such a condition. The disease should be suspected in the case of any person recently returned from an endemic zone of infection, who presents the signs and symptoms of a respiratory infection. If a positive coccidioidin test is obtained under these circumstances, a presumptive diagnosis of coccidioidomycosis is warranted. A negative test rules out the disease in all but the most severe infections. The diagnosis is established with certainty by a positive complement-fixation or precipitin test or by recovery of the causative organism from the sputum by culture or guinea-pig inoculation.

2. In the acute pneumonic phase of the disease, the roentgen appearance is nonspecific, and differentiation from primary atypical pneumonia, rheumatic pneumonitis, and other respiratory infections cannot ordinarily be made from the roentgenograms alone.

3. Residual "burned-out" nodular or cyst-like foci of coccidioidomycosis are quite characteristic in roentgen appearance and are seldom confused with other conditions when occurring in endemic areas. Among diseases to be differentiated are primary tuberculosis, metastatic carcinoma, congenital cyst, adult tuberculosis, lung abscess, pyogenic and mycotic infections. The discrepancy between the clini-

cal and roentgen findings is often helpful in establishing the diagnosis.

4. Cases in which mediastinal adenopathy is dominant are usually among the more severe and prolonged of infections and give rise to most of the fatalities. Among the conditions to be considered in the differential diagnosis are Hodgkin's disease, pulmonary tuberculosis, sarcoidosis, and bronchiogenic carcinoma.

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Pulmonary Sarcoidosis: The Early Roentgen Findings[1]

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THE PULMONARY changes in sarcoidosis are now recognized as constituting one of the most conspicuous manifestations of this bizarre and no longer rare disease. They are usually described as being of one of the following types: (*a*) lymph node enlargement, (*b*) miliary or nodular lung densities, or (*c*) a combination of nodal enlargement and pulmonary infiltration. Are there any particular lesions suggestive or characteristic of *early* pulmonary sarcoid disease? In an attempt to determine this point, we studied a series of cases of sarcoidosis which we have been privileged to see during the last several years (33 of which were proved by biopsy or necropsy) and reviewed much of the now voluminous literature on the subject. Since sarcoidosis is a disease of protean manifestations and constant changeability, we believe it will be well to consider briefly its salient features before analyzing the purely pulmonic aspects.

CLINICAL ASPECTS OF SARCOIDOSIS

Sarcoidosis is a generalized disease of unknown origin, in which characteristic histologic changes are found in different organs and tissues (17, 19). It is usually of insidious onset and tends to run a chronic, relapsing course. Fairly mild constitutional symptoms are manifested in most cases, and quite severe, even fatal, signs in a few. It is discovered most commonly between the ages of twenty and thirty years, but cases have been reported in patients as young as two months (19) and as old as eighty years (11). It may develop in persons of any race, but *seems* to occur with somewhat greater frequency in Negroes than in others (12, 13, 14).

Although a widespread, disseminated disease, it is often observed in a phase when involvement of only one system is apparent; for example, lesions of the skin, the eyes, or the lungs. The clinical picture varies from case to case, and from time to time in the same case. The victims may have no complaint or may complain of fever, fatigue, or slight dyspnea. Peripheral lymphadenopathy is present at some stage of the disease in about 90 per cent of cases, the nodes being painless, discrete, and movable. Pulmonary involvement (parenchymal or nodal) occurs in a similar percentage of cases. Cutaneous and ocular lesions are seen in about 40 per cent of cases. The usual skin lesions are described as sharply defined, brownish nodules (cutaneous or subcutaneous) distributed over the face or extremities (12). The common ocular finding is a chronic bilateral granulomatous iritis, or iridocyclitis, without much redness or pain. This may regress spontaneously or progress to complete blindness. Hepatomegaly and splenomegaly are fairly frequent. Cardiac and pericardial involvement has been noted. As in Hodgkin's disease, *any* tissue or structure can be invaded.

Infiltration of the salivary apparatus may lead to "Mikulicz's disease," and of the parotid glands and eyes to "uveo-parotid fever." Granulomatous invasion of the bone marrow is fairly common, but roentgenographic evidence of such is noted only in a small percentage of cases (7), appearing either as multiple radiolucent areas or diffuse lace-like rarefactions. These are most common in the phalanges of the hands and feet, but may occur in any bones, notably the long bones of the extremities. Hyperglobulinemia, with reversal of the albumin-globulin ratio, is a common finding; eosinophilia is not infrequent. The serum calcium and phospha-

[1] Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1–6, 1946.

tase values may be slightly increased (8, 19, 20).

The tuberculin reaction is usually negative. A certain number of cases, however, are eventually complicated by tuberculosis or other serious infection, especially in their terminal stages (15, 17). The diagnosis is made *in vivo* by the demonstration of a non-caseating or "hard" tubercle in a biopsy specimen, usually from a node or skin nodule. The conditions with which sarcoidosis is most often confused are tuberculosis and Hodgkin's disease.

HISTORICAL NOTE

The skin changes of sarcoidosis were described in 1889 by Besnier (3), who designated them lupus pernio, and in the same year by Boeck (4), who called them sarcoid. The latter term was used because the author considered that they might be related to the sarcomata or pseudoleukemic disorders; in 1901 he changed the name to benign miliary lupoid, and in 1905 stressed the fact that the lesions were also found in mucosal tissues, lymph nodes, and internal viscera. In 1916, Schaumann (16) emphasized the histologic identity of the lesions of lupus pernio and miliary lupoid and stressed the fact that they were of widespread occurrence throughout the body. Other writers (6, 11, 19) have described conditions or syndromes involving certain areas or tissues (such as Mikulicz's disease, Heerfordt's syndrome), all of which are now known to be merely manifestations of sarcoidosis. Synonyms include benign lymphogranulomatosis, reticulosis, and reticuloendotheliosis.

The bone changes of sarcoidosis were first described by Jüngling in 1919 as "osteitis tuberculosa multiplex cystica" of the phalanges; nine years later he changed the term to "osteitis tuberculosa multiplex cystoides." Finally, it was recognized that the changes were due to sarcoid infiltration of the bone marrow and, like other sarcoid lesions, were reversible (though fibrotic changes persisted in the marrow of arrested cases) (20).

HISTOLOGIC CHANGES

The essential lesion of Boeck's sarcoidosis is a miliary tubercle composed of a central giant cell surrounded by epithelioid cells and lymphocytes, the giant cell sometimes containing an asteroid body. No perituberculous inflammatory reaction, caseous necrosis, or calcification occurs, thereby distinguishing the sarcoid tubercle from the true tuberculous tubercle. In addition, of course, tubercle bacilli are frequently found in the tuberculous tubercle, and never in the uncomplicated sarcoid tubercle. The sarcoid tubercle has a tendency to undergo hyalinization and fibrosis.

Carnes (5) has emphasized that the following diseases require differentiation from sarcoid on the basis of lymph-node examination alone: (*a*) non-caseating pulmonary tuberculosis; (*b*) leprosy (tuberculid form); (*c*) syphilis; (*d*) fungous infections, as coccidioidomycosis; (*e*) tularemia; (*f*) lymphopathia venereum. He points out that consideration of the clinical findings, plus the result of suitable antigen tests (tuberculin and lepromin skin reactions, serological examination, coccidioidin and Frei tests, etc.) will help the clinician to distinguish these entities.

Gross and microscopic lesions similar to those in sarcoid have been found (22) in some zinc-beryllium-silicate workers (fluorescent lamp manufacturers, etc.).

Williams and Nickerson (22), Snapper (17), and others (11) have suggested that the disease may be due to a virus; they are convinced that it is *not* due to any form of the tubercle bacillus. On the other hand, Pinner (13) considers that it is a bizarre form of tuberculosis. Thomas (20) lists seven authors who claim to have found tubercle bacilli in "sarcoid lesions" (and five who reported "sarcoids" in leprosy!). Snapper observes that "this cannot be considered proof of a tuberculous etiology, since in diabetes mellitus, Hodgkin's disease, and leprosy a terminal tuberculosis is not infrequent."

PULMONARY FINDINGS REPORTED IN THE LITERATURE

(*a*) *Pathologic:* The microscopic changes in the lungs of persons with sarcoidosis consist of diffuse, non-caseating tubercles in the periadventitial layers of the smaller arteries in the interalveolar septa, with variable degrees of fibrous degeneration (17). The latter may progress to obliteration of the interalveolar pulmonary capillaries. The lymph nodes and lymphatic structures of the mediastinal, hilar, and pulmonary tissues show more or less invasion by these tubercles, with swelling or fibrosis, depending on the stage of involvement. As Pinner (13) remarks, "there is not only uniformity, but monotony in regard to the histologic findings in this disease." The predilection of sarcoids for the lymphatic structures of the interlobular septa explains the diffuse streaking so often seen in pulmonary roentgenograms, according to Bernstein and Sussmann (2). Sarcoid fibrous tissue may ultimately replace the pulmonary lymphoid structures.

Readers interested in viewing excellent reproductions of the gross and microscopic changes produced by sarcoid lesions in the lungs, heart, and other viscera, are referred to Cotter's (6) and Tice and Sweany's (21) illuminating articles on this subject.

(*b*) *Roentgenologic:* The descriptions of the various roentgenologic changes in the lungs of persons with sarcoidosis are as varied as the protean manifestations of the disease. This is due partly to the fact that individual cases are seen at certain phases of the disease with widely variable degrees of lung or lymph node involvement, and partly to inadequacies in our roentgenologic descriptive terminology.

Snapper (17) described (*a*) disseminated pulmonary nodulation, (*b*) diffuse interstitial fibrosis, and (*c*) lobar collapse from hilum adenopathy. This adenopathy was often of severe degree ("potato nodes"). Both lung and node lesions might disappear or might persist for many years. Four of 13 cases were followed for five to twenty years, and extensive lesions which regressed did not recur. Snapper did not indicate his impression as to which constituted the early roentgen findings.

Longcope and Pierson (11) noted similar changes in 8 cases, and re-emphasized the changeability of the pulmonary findings from year to year.

Spencer and Warren (18) maintained that certain "characteristic" changes in the lungs occurred in this disease.

Tice and Sweany (21) reported a fatal case of pulmonary sarcoidosis, in which, incidentally, the successive clinical diagnoses during life were pulmonary tuberculosis, Hodgkin's disease, Ayerza's disease, and mediastinal tumor. In their opinion, "the early lung lesions appear on the roentgenogram usually as nodules simulating disseminated tubercles, or small soft infiltrates with an associated hilum lymph node enlargement.... As the lesions become chronic, there is a disappearance of their 'soft' nature and the appearance of a stringy and net-like fibrosis over the entire lung fields, especially out from the hilum. A late emphysema usually appears."

Kerley (9), in a discussion on erythema nodosum and sarcoidosis, described the changes as of two general types: (*a*) pulmonary nodular infiltrate, with lesions averaging 3.0 mm. in diameter, and (*b*) a coarse reticular striation radiating from the hila. He observed that both types are usually present together and that, in about 50 per cent of cases, hilar adenopathy also occurs, "the adenopathy appearing and regressing often in a very short time, for example in three to five days!" He regards the "erythema-nodosum-sarcoidosis" of Europe as being closely related to, if not identical with, the "erythema-nodosum-coccidioidomycosis" of California!

Thomas (20) reported 15 cases of sarcoidosis, with pulmonary involvement in most of them; there were 3 deaths, one due to pulmonary tuberculosis developing within a year after the sarcoids first appeared, one to massive pulmonary infarction as a result of hilar node pressure, and one to amyloidosis some four years after the sarcoidosis appeared. Of the remain-

ing 12 cases, 7 persisted unchanged, and 5 spontaneously recovered from all detectable lesions.

King (10) discussed a group of 50 cases from the point of view of chest roentgenography, some 24 of them proved by biopsy of skin or lymph nodes. He classified the lesions as falling into various patterns, such as hilar node enlargement, miliary pulmonary changes, etc. He stated that in none of his cases did fibrotic changes develop (or right heart failure secondary to such changes). Many cleared completely, the average time for clearing being twenty-two months. King did not comment on the possible pattern of the earlier lesions.

Reisner (14), in a comprehensive review of 35 biopsy-proved cases followed for an average period of 4.3 years, observed pulmonary involvement at some time in 33 of them. In many instances the chest findings were discovered on routine x-ray examination or in mass surveys of apparently well persons. In half of the cases—17—lymphadenopathy and pulmonary involvement were the only demonstrable findings. There was no correlation between the extent of involvement and the subjective symptoms. The roentgen findings were described as usually bilateral and diffuse, but occasionally unilateral and localized. They predominated in the lower two-thirds of the lungs. None was pathognomonic.

Reisner found (*a*) diffuse miliary or nodular lesions in about one-third of the cases, (*b*) linear accentuation of the bronchovascular markings, usually with nodulation, in another third, and (*c*) localized or pneumonic infiltrates in the remainder. He regarded the miliary-like, disseminated, nodular form as an early stage of the disease. "Of 10 patients in whom the pulmonary changes became manifest during the course of observation, 8 presented lesions of the diffusely disseminated type." The linear, interstitial, fibrotic form and the conglomerate type were regarded as intermediate or late stages and, in contrast to the former, usually irreversible. Incidentally, 4 of the cases developed as complications of pulmonary tuberculosis, with positive sputum; two additional patients died of generalized tuberculosis, without manifest pulmonary infection *in vivo*.

The mediastinal and hilar nodes were involved in most of Reisner's cases, usually bilaterally. Spontaneous regression, during a period of several months or years, occurred in half of these. Of the entire group, 27 were followed long enough to permit some estimate as to their behavior; 5 remained *stationary*—usually the linear fibrotic or confluent density type—some showing alternating remissions and exacerbations; 9 showed *progression*, usually to conglomerate densities, often with fibrosis, bronchiectasis, and emphysema; 13 showed *regression*—usually the disseminated miliary or nodular type—some with complete clearing.

Bernstein and Sussmann (2) reported 12 cases proved by histologic examination. They divided the roentgen findings into five groups: (*a*) enlarged hilar nodes without evident pulmonary infiltration; (*b*) mediastinal adenopathy with variable degrees of pulmonary infiltration; (*c*) miliary pulmonary lesions (with or without mediastinal adenopathy); (*d*) discrete nodular infiltrates (with or without hilar adenopathy); (*e*) diffuse confluent infiltrations.

Bernstein (1), in a subsequent paper on the miliary form of the disease, divided the intrinsic pulmonary lesions into three groups: (*a*) a diffuse linear, strand-like pattern, often with hilar adenopathy; (*b*) diffuse, patchy, or confluent densities; (*c*) miliary forms, either diffuse or limited to the lower two-thirds of each lung. Transitions from one type of infiltration to another were often noted under prolonged observation. Bernstein is in agreement with Reisner that cases with the shortest duration of symptoms tend to show a miliary distribution; many of them regress spontaneously. The linear or conglomerate forms tend to persist, with development of fibrosis.

Several other writers have described from one to as many as nine cases of sar-

coidosis, with variable degrees of pulmonary involvement. None of these considered the disorder from the specific point of view of early chest findings, and reference to them is therefore omitted in this paper.

AUTHOR'S SERIES

We are reporting in this paper the chest roentgenographic findings in 36 cases of sarcoidosis, 33 of which were verified by histologic examination, and 3 of which were so well established clinically that the validity of the diagnosis appears unquestionable. Several of these, as in Reisner's series, were discovered incidentally in routine chest x-ray examinations of apparently healthy persons. Two of them were found during fluoroscopic examination of the gastro-intestinal tract because of mild abdominal complaints. Most of the cases were subjected to extensive clinical and laboratory examination in order to rule out other diseases, notably tuberculosis, coccidioidomycosis, histoplasmosis, Hodgkin's disease, and syphilis. A few were observed sufficiently soon after negative roentgen examinations elsewhere to warrant assumption that the pulmonary findings were truly early.

The following were the salient findings in our group as a whole:

Age, Sex, and Nationality: The ages ranged from 11 to 74 years, slightly over half of the patients being in the twenties. There were 14 males and 22 females. Twenty-one patients were white and 15 colored, the latter group consisting of 1 Puerto Rican and 14 American-born negroes. All of the whites on whom natal data were available were born in this country.

It is probable that the average age, sex, and nationality depend largely upon the material analyzed. At our City Hospital, many of the patients are middle-aged or elderly white females; the sarcoid cases from this institution were of similar composition. At the Oakland Naval Hospital, many of the patients were young males; the sarcoid cases encountered there were of a similar type. However, as other observers have noted, negroes do show a proportionately greater tendency to involvement than whites.

Initial Roentgen Findings: The thoracic roentgen findings may be divided into those showing apparent involvement of the lungs alone, those indicative of lung and lymph node involvement, and those apparently indicating lymphadenopathy alone. The pattern of the lung involvement is extremely variable, ranging from true miliary densities, through coarse nodulation and apparent linear fibrosis, to coalescent cirrhotic or pneumonic shadows, all with or without adenopathy. There is absolutely nothing characteristic in the findings in the individual case; however, the apparent excellent health of the person in contrast with the extensive roentgen shadows often warrants a surmise as to the nature of the latter. The miliary and nodular lesions are due to aggregations of sarcoids in the lung parenchyma. The linear lesions may be due to sarcoid lymphangitis, to lymphedema, to congestion or, occasionally, to fibrotic changes.

Pulmonary lesions alone, without visible hilar or mediastinal adenopathy, were present at the initial examination in 10 cases. One showed disseminated miliary lesions, that is, parenchymal densities of about 1 mm. diameter. Four showed diffuse or localized nodulation—parenchymal densities varying from 1 to 5 mm. in diameter, mostly about 3 mm. Four showed linear shadows, usually irregular and "fibrotic" looking. One showed coalescent bronchopneumonic-like lesions.

Pulmonary lesions and lymphadenopathy were present at the initial examination in 13 cases. Six showed diffuse or localized nodular lesions with adenopathy, while 7 showed diffuse or localized linear densities with adenopathy.

Lymphadenopathy, hilar, mediastinal, or both, was present as the sole thoracic roentgen finding at the initial examination in 11 cases. Six showed bilateral hilar plus *right* paratracheal adenopathy; 3 showed hilar adenopathy alone; and 1 each

TABLE I: INITIAL OR FIRST NOTED PULMONARY ROENTGEN FINDINGS

(Author's Series. All Cases, Both Early and Late)

Roentgen Findings	Case Numbers*	Total
Pulmonary lesions alone		
Disseminated miliary type densities	32	1
Diffuse nodular densities	28, 36	2
Localized nodular infiltration	2, 26	2
Diffuse or localized linear densities (fibrotic type)	3, 17, 18, 33	4
Patchy coalescent densities	1	1
Pulmonary and nodal lesions		
Diffuse or localized nodular densities with nodes	*5, 12, 23, 27,* 29, 34	6
Diffuse or localized linear densities with nodes	8, 10, *13, 19, 20,* 30, *31*	7
Nodal lesions alone		
Bilateral hilar and right paratracheal adenopathy	*9, 14, 21, 22, 24, 35*	6
Hilar adenopathy alone	4, 11, 25	3
Paratracheal adenopathy	6	1
Other (*e.g.*, hilar and left paratracheal adenopathy)	15	1
NOTE: The lungs were clear in Case 7 at initial examination and at necropsy. They were also clear in Case 16 at first; later hilar and paratracheal adenopathy developed.		1
		1
		36

* Cases designated by italic numbers showed a "sarcoid-type" of lymph node change, *i.e.*, bilateral hilar and right paratracheal adenopathy.

paratracheal adenopathy alone, and hilar plus left paratracheal adenopathy.

There were two patients without thoracic roentgen findings at the initial examination; one died shortly thereafter of generalized sarcoidosis; in the other hilar adenopathy developed after three weeks' observation.

Pleural thickening was noted in only one case at the initial examination, and developed subsequently in one other. Pleural effusion was present in only one case.

The intrathoracic lymph node enlargement tended to conform to a curious pattern in 13 of the 24 cases showing adenopathy. We have not seen this observation recorded previously in the literature and we are stressing it at this time because we believe it may be of suggestive diagnostic value in some cases. The pattern was one in which there was simultaneous enlargement of *both sets of hilar nodes* and only the *right upper mediastinal or paratracheal nodes*. This occurred in 7 of the cases with combined parenchymal and nodal lesions, and in 6 of the cases with nodal lesions alone. We have been led to regard this as suggestive of "sarcoid-type" adenopathy (see Fig. 8 for typical example).

As far as *symptoms* referable to the thoracic area were concerned, only 6 patients complained of these at the initial examination, and in only about three others did any such symptoms develop during the entire period of observation.

The *course* of the cases showed wide variation: in 10 there was evidence of regression or complete clearing of the lesions during a period of six months to three years; in 4 the lesions remained stationary for periods up to seven years; in 3 there was progression of the lesions during periods up to six years. Nineteen cases were followed for less than six months and, therefore, are regarded as under observation too short a time to permit statements as to progress.

TABLE II: BEHAVIOR OF PULMONARY LESIONS UNDER SERIAL OBSERVATION

(Author's Series)

1.	No. of cases showing *regression* of lesions during period of 6 months up to 3 years	10
2.	No. of cases in which lesions were *stationary:* observation period, 6 months to 7 years	4
3.	No. showing *progression* of lesions during period of 6 months to 6 years	3
4.	Observation period too short (less than 6 months)	19

NOTE: Some cases showed alternate regression and progression of both parenchymal and nodal lesions, occasionally after years of stationary behavior. Therefore, the observations in this table, even those of 7 years' duration, cannot be regarded as final.

EARLY ROENTGEN FINDINGS

The nature of the "primary" or, if such exists, "first re-infection type" sarcoid lesion in the lungs is not yet established. The author has previously referred to several writers who have expressed the opinion that the early pulmonary lesion is a diffuse miliary one. Reisner (14) states

that he observed the development of such lesions in 8 out of 10 cases in which the pulmonary changes became manifest during the course of observation.

We reviewed our material in an attempt to establish certain cases as early. While some 30 patients had no pulmonary symptoms (6 being discovered on routine chest survey of apparently healthy persons), only 2 had well established negative clinical histories and negative roentgen examinations for a period of weeks or months prior to our initial examination. In one of these 2 cases (Case 16) hilar and right paratracheal *adenopathy* developed while the patient was under observation, and in the other (Case 28) *bilateral nodular parenchymal lesions* developed, more marked in the right lung. In neither of our well established early cases, therefore, was there a miliary pulmonary pattern.

However, in the 6 cases encountered in "healthy" persons, and in 6 additional cases in which pulmonary symptoms were absent and clinical signs of disease elsewhere in the body were of only a few days' or weeks' duration (Cases 5, 19, 20, 21, 22, 23, 26, 27, 30, 32, 35, and 36), the following findings were observed:

	Cases
Disseminated miliary pulmonary lesions	1
Diffuse or localized nodular lesions	2
Nodular densities with adenopathy	3
Linear densities with adenopathy	3
Adenopathy alone	3

All of these cases may reasonably be regarded as early ones, even though previous negative chest films are not always available to establish them as positively so. It will be noted that only 1 showed miliary disease, while 8 showed nodular or linear densities.

If we tabulate the 2 definite with the 12 probable early cases, we observe the following roentgen findings as the first established ones:

Disseminated miliary lesions	1
Nodular lesions (diffuse or localized)	3
Nodular or linear parenchymal densities with adenopathy	6
Adenopathy alone	4

On the other hand, if we follow cases over a long period of time, we encounter some (such as Case 9) in which a miliary or "granular-type" of parenchymal lesion develops as an apparent extension of a preexisting localized lymph nodal or pulmonary nodular process. It is, therefore, our impression that there is more chance of the primary pulmonary manifestation of sarcoidosis being one of combined parenchymal densities plus lymphadenopathy than of being purely a miliary parenchymal process.

TABLE III: EARLY PULMONARY ROENTGEN FINDINGS IN SARCOIDOSIS
(Author's Series)

	Cases
Disseminated miliary parenchymal lesions	1
Diffuse or localized nodular parenchymal lesions	3
Parenchymal lesions with adenopathy (usually bilateral hilar and right paratracheal)	6
Adenopathy alone (hilar and right paratracheal)	4

DIFFERENTIAL ROENTGEN DIAGNOSIS

The differential diagnosis of pulmonary sarcoidosis requires consideration of so many lesions of similar gross anatomic pattern that it is manifestly impossible on the basis of a single roentgen examination alone. The following are some of the conditions which may simulate the disease: (*a*) miliary pulmonary disease of any type, such as tuberculosis, coccidioidomycosis, carcinosis, etc.; (*b*) nodular pulmonary disease of any type, such as pneumoconiosis, severe chronic passive congestion, Ayerza's disease, leukemia, virus or coccal pneumonitis, viral pneumonia, eosinophilia, bronchopneumonia, periarteritis nodosa, byssinosis, schistosomiasis, and fungous infections; (*c*) parenchymal infiltrative or fibrotic disease, such as chronic fibroid tuberculosis, lymphoblastoma, roentgen pneumonitis, paragonimiasis, etc.; (*d*) mediastinal and hilar disease, as tuberculous adenopathy, lymphoblastoma (Hodgkin's type especially), aneurysmal dilatation of the pulmonary arteries, etc.

These various conditions can often be excluded on clinical and other grounds. Skin tests for many of the entities are help-

ful. Histologic study of a removed node is often decisive. Despite the absence of pathognomonic findings in general, we are convinced that there are certain patterns quite suggestive of pulmonary sarcoidosis, if information on the clinical status of the patient is at hand. In order of frequency, these are:

(*a*) Bilateral hilar and right paratracheal adenopathy, with or without associated pulmonary infiltration or nodular densities.

(*b*) Widely disseminated pulmonary miliary or nodular densities without calcification, in a person clinically well.

(*c*) Massive enlarged hilar nodes (potato nodes) in an apparently well person.

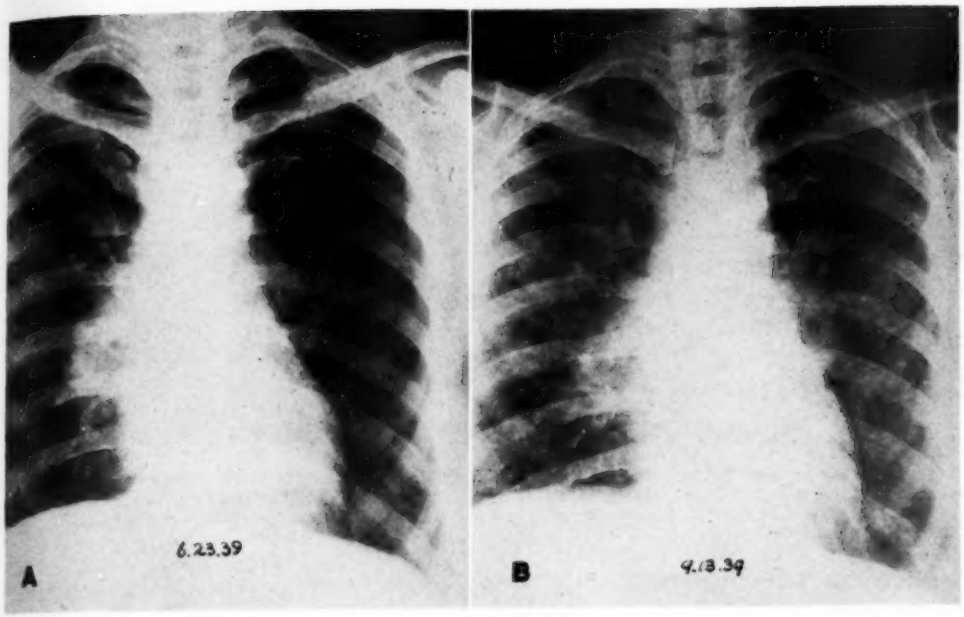
The presence of associated lesions in the peripheral nodes, skin, and uveal tract is obviously of diagnostic value to the alert clinician. Bone lesions are often stressed, but those of a classical cystic type are reported in only about 10 per cent of the cases occurring in this country. We believe, however, that porotic changes are visible in some of the phalanges or long bones of the hands and feet in at least an additional 10 per cent. These "*coarse trabeculae with cortical thinning*" may be due to a host of other conditions but, in association with pertinent thoracic findings, are of diagnostic value to the radiologist. In sarcoidosis, they are due to infiltration of the marrow with hard tubercles and fibrous tissue.

CASE REPORTS

Introductory Note: For purpose of brevity, only positive findings will be listed in the following case reports. Thus, in a given case, skin lesions, enlarged nodes, ocular disease, etc., may be regarded as absent or not detected if not specifically mentioned. The blood Wassermann test was negative except as noted. *Tuberculin tests* were performed in most cases, usually down to dilutions of 1:10; coccidioidin tests to 1:100; histoplasmin tests in the standard dilution currently available: all of these tests were negative except as indicated in two instances. Examination of sputum and/or gastric washings for tubercle bacilli was performed in all cases (often ten or more times over a period of weeks or years), and was *negative* except in one questionable instance. Guinea-pig inoculations were made in many cases without resulting tuberculosis. Agglutination tests for typhoid, paratyphoid, brucellosis, tularemia, and other disorders were made in a few cases and were uniformly negative. The blood counts were usually normal, except for occasional eosinophilia; neither they nor the urine examinations will be recorded in these summaries except when abnormal. Albumin-globulin ratios[2] were determined in 15 instances; blood calcium and serum phosphatase levels in only a few cases. X-ray examination of the hands or feet was negative except as otherwise noted. Most of the histologic studies were made by Drs. D. A. Wood or A. J. Cox of Stanford University Medical School; some were done by Dr. J. L. Carr, and by other experienced pathologists. To all of these able workers we wish to record our deep appreciation. Their biopsy reports usually listed such findings as "Many small tubercles, made up of epithelioid cells and a scattering of lymphocytes; most contain one or more giant cells. There is no central necrosis. Some fibrosis is present about the tubercles. Asteroid bodies are (or are not) present. No acid-fast organisms are found. Conclusion: Non-caseating granuloma." These reports we have condensed to "sarcoid" (*Boeck's*), in view of the associated clinical and laboratory data which we list. Specific skin tests for sarcoidosis have not been of value in our series.

CASE 1: C. F., white, male, 27. Cough and progressive weakness for three months. Roentgen findings: enlarged heart; bilateral confluent densities in lower two-thirds of lungs (? bronchopneumonia or fungous infection). Clinical diagnosis: lymphosarcoma or bronchopneumonia. Sudden death. Necropsy findings: miliary tubercles scattered throughout lungs, confluent in lower two-

[2] Hyperglobulinemia and a reversed albumin-globulin ratio are often found in sarcoidosis. The normal serum proteins range from 6 to 8 mg. per cent; the normal albumin from 3.8 to 5.5 mg.; and globulin from 1.5 to 3.5 mg. The standard A-G ratio is usually given as 1.7 to 1.



thirds, grossly resembling a tuberculous bronchopneumonia. Microscopically, non-caseating miliary tubercles, without calcification or bacilli. Heart enlarged; old aortic stenosis, with fresh vegetations on one valve. No definite tubercles in myocardium.

Summary: A white male with clinical diagnosis of lymphosarcoma, and necropsy diagnosis of pulmonary sarcoidosis, diffuse, confluent stage.

CASE 2: E. F., white, female, 50. Dyspnea for two years; swollen fingers for eleven months. History of old "lupus vulgaris" of face, and skin "tuberculid" on left forearm. Roentgen findings: slight nodular infiltration in lower lobe of right lung; extensive cystic and porotic changes in phalanges of hands. Clinical diagnosis: arteriosclerosis and bronchial asthma. Biopsy of skin nodule showed cluster of epithelioid cells and some giant cells; no caseation or bacilli. Course: unimproved.

Summary: A white female with pulmonary symptoms out of proportion to the slight roentgen changes, and classical sarcoid soft-tissue and bone changes in the hands. She may have had myocardial sarcoidosis as the principal lesion.

CASE 3: V. T., white, female, 44. Weakness, and painless mass in left upper abdominal area for eight weeks. Malaria at age 5, typhoid at 16, influenza at 24. Tuberculin and coccidioidin tests negative. Roentgen findings: bilateral fibrotic-like densities in the lower two-thirds of the lungs; hands negative. Clinical diagnosis: splenomegaly. Laparotomy and biopsy of spleen and abdominal nodes; non-caseating tubercles. Course: slow

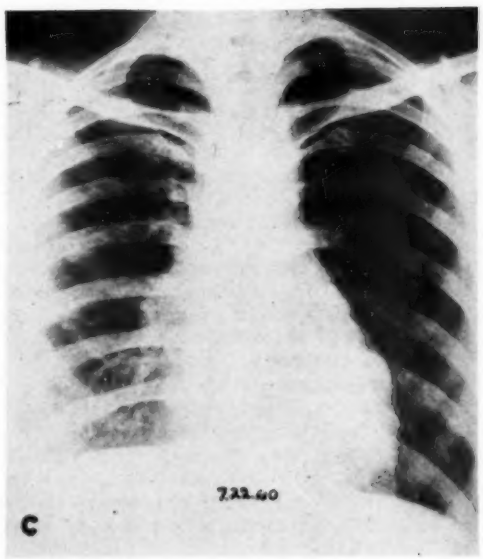


Fig. 1. Case 5: Pulmonary sarcoidosis. "Classical" course with spontaneous improvement. White, female, 47, with erythema nodosum and no pulmonary symptoms. Positive skin biopsy.

A. Bilateral hilar adenopathy with slight pulmonary nodular infiltration.

B. Bilateral pulmonary "fibrotic" and nodular changes; right basal pleural thickening.

C. Marked improvement. (June 1939 to July 1940.)

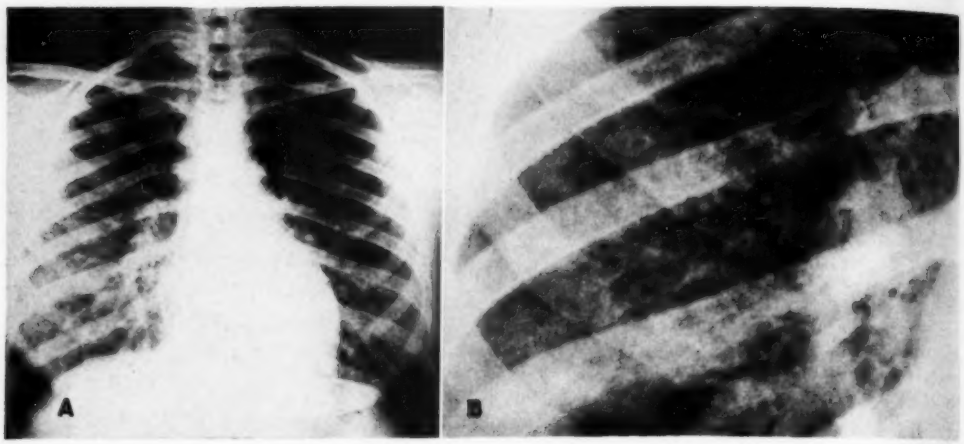


Fig. 2. Case 9: Sarcoidosis. Granular, pseudo-miliary pulmonary infiltrate developing relatively late in the disease. White, female, 17, who, six years and a half previously, had bilateral hilar and right paratracheal adenopathy. Positive skin biopsy. See case report in text for details of serial roentgen examinations, etc. B. Detail view of granular infiltrate (pseudo-miliary).

improvement. Three years later chest about 33 per cent better.

Summary: A white female with splenomegaly, abdominal lymphadenopathy, and chronic pulmonary disease, due to sarcoidosis. (Three-year follow-up.)

CASE 4: M. E., white, female, 18. Severe headache for six weeks; one episode of severe abdominal cramps two months ago; recent "swelling of right eyeball." Tuberculin, coccidioidin, and Frei tests negative. Roentgen findings: slight, questionable left hilar adenopathy; skull negative. Clinical diagnosis: possible multiple sclerosis. Course: rapid blindness of right eye; orbital decompression without benefit; tissue about optic nerve removed and reported "inflammatory tissue." One year later, iridocyclitis in left eye. Four years later, appearance of an abdominal mass; laparotomy disclosing enlarged prepancreatic nodes (histologically, non-caseating tubercles). Then sudden blindness of left eye. Two years later, slight improvement in this eye. Patient can now distinguish light and darkness. Chest film stationary; lung parenchyma always clear.

Summary: A young white female, with meningeal, ocular, and abdominal sarcoidosis and blindness. (Eight-year follow-up.)

CASE 5: A. B., white, female, 47. Painful swellings about the ankles; subcutaneous nodules on the chest and arms. Roentgen findings: bilateral hilar adenopathy with slight pulmonary nodular infiltration. Clinical diagnosis: erythema nodosum. Biopsy of subcutaneous nodule from left elbow, showing sarcoid. A-G ratio: 3.76:3.31. One year later, marked spontaneous improvement.

Summary: A white female with erythema nodosum, skin nodules, and chronic lung changes due to sarcoid.

CASE 6: C. C., white, male, 40. Bilateral facial palsy for ten weeks; swollen parotid glands; history of radiation therapy to mediastinum for Hodgkin's disease five months previously. Roentgen findings: bilateral paratracheal adenopathy; lung parenchyma negative. Biopsy of left epitrochlear node showing sarcoid. A-G ratio: 4.08:2.35. Five months later, chest almost clear. One year later, bilateral upper lobe infiltrate. Palsy improved. Hands negative initially, but four years later showed phalangeal cyst-like areas. Patchy phalangeal osteoporosis developed in feet, also. Left facial palsy recurred after four years, with dizziness, parotitis, etc.

Summary: A white male with chronic, intermittent, meningeal, nerve, lung, and bone changes due to sarcoid. (Four-year follow-up.)

CASE 7: A. H., white, female, 67. Weakness for seven months; cough and nasal discharge for three months. Bilateral parotitis. Roentgen findings: chest negative. Biopsy of parotid gland: granuloma. Progressive downhill course. Necropsy: granulomatous lesions, with non-caseating miliary tubercles in the kidneys, liver, nasal cartilages, and pituitary gland.

Summary: An elderly white female with generalized sarcoidosis, which spared the lungs and bones, as far as could be determined during the brief period of observation and at necropsy.

CASE 8: C. D., white, female, 45. Chronic "eye trouble." Brownish, indurated nodules on the skin of the arms and legs for three months. Roentgen findings: slight bilateral hilar adenopathy and pul-

monary "fibrotic" infiltration. Hands: coarse trabeculae in phalanges. Clinical diagnosis: iridocyclitis, chronic, bilateral. Biopsy of skin nodule: sarcoid. Course not known.

Summary: A white female with sarcoidosis of the skin, eyes, lungs, and bones.

CASE 9: B. H., white, female, 13. "Rough areas on skin" of face and forearms for four years. Roentgen findings: marked bilateral hilar and slight right paratracheal adenopathy; lungs virtually clear. Over a period of two years, nodes receded partly, and nodular pulmonary infiltrate developed. Hands and feet showed bone changes. Biopsy of skin nodule: sarcoid. A-G ratio: 3.98:3.4. Course: gradual improvement. Six years later, some skin lesions still present. Disseminated miliary type of pulmonary lesions present; hilar nodes gone. The following is a condensed summary of the serial roentgen findings in the chest:

7-29-40: Marked hilar and slight right paratracheal adenopathy; lungs virtually clear; diagnosed tuberculous adenitis.

2-8-41: Nodes smaller; slight bilateral perihilar infiltration.

11-1-41: Nodes larger; nodular infiltration in middle third of each lung.

10-1-42: Nodes larger (bilateral hilar and right paratracheal, marked); infiltration now in right upper lobe.

1-8-44: Nodes smaller; nodular infiltration much more extensive, especially on the right.

6-6-45: Nodes smaller (only right paratracheal nodes evident); pulmonary nodulation slightly coarser.

11-2-46: Diffuse, fine granular infiltration in middle three-quarters of each lung.

Between 1943 and 1945, both cyst-like and porotic (lacy) changes were visible in a few of the phalanges of the hands and feet. The intracutaneous sarcoids also persisted.

Summary: A young girl with cutaneous, pulmonary, and osseous sarcoidosis, chronic.

CASE 10: G. G., colored, female, 42. Weakness and marked loss of weight, eight months. Slight adenopathy. Roentgen findings: bilateral hilar adenopathy; perihilar infiltration or lymphangitis. Biopsy of node: sarcoid. A-G ratio: 4.42:5.68. Course unknown.

Summary: A female negro with pulmonary sarcoidosis and marked weight loss.

CASE 11: A. B., white, female, 50. Bilateral facial palsy, deafness, eye trouble, and swollen glands. Skin lesions on arms. Roentgen findings: bilateral hilar adenopathy, marked. Clinical diagnosis: ? sarcoid, with iridocyclitis, etc. Biopsy of skin nodule: sarcoid. Course unknown.

Summary: A white female with sarcoidosis of the meninges or cranial nerves, eyes, parotids, skin, and lungs.

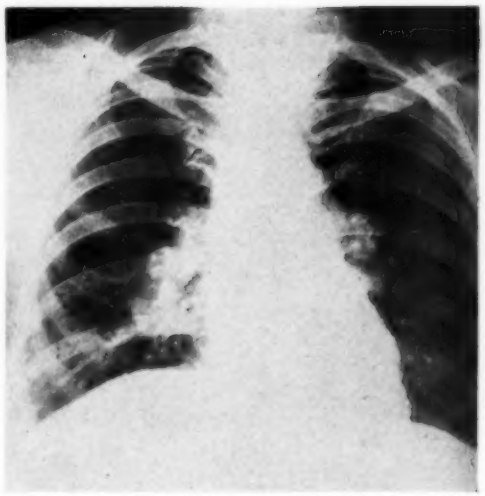


Fig. 3. Case 11: Sarcoidosis. Enlarged hilar nodes. White, female, 50, with facial palsy, deafness, iridocyclitis, and parotitis. Positive skin biopsy.

CASE 12: G. J., colored, male, 25. Failing vision in the left eye. Clinical examination disclosed iridocyclitis, cervical adenopathy, parotid swelling, and intracutaneous nodules on the forearms. Roentgen findings: slight hilar and marked right mediastinal adenopathy; slight nodular infiltration in lower one-third of each lung. Clinical diagnosis: sarcoid. Biopsy of skin nodules: sarcoid. A-G ratio: 3.7:3.3. Two years later, chest clear, but skin and eye lesions unchanged.

Summary: A young negro with chronic ocular and cutaneous sarcoidosis and transient pulmonary and parotid disease. (Two-year follow-up.)

CASE 13: R. G., white, male, 28. "Sore eyes" for six months. Treated for chronic right iritis. Roentgen findings: hilar and right mediastinal adenopathy; slight pulmonary congestion or infiltration. Hands and feet negative. Clinical diagnosis: possible tuberculosis. Three months later, chest and eye improved. Five months later, eye negative; hilar adenopathy improved; parenchymal infiltrate extending. Two years later, caught cold. Chest x-ray interpreted (elsewhere) as far-advanced tuberculosis. Multiple sputum and other tests negative. Clinical diagnosis: tuberculosis or lymphogranuloma.

Despite the absence of palpable nodes, Drs. D. L. Wilbur and A. C. Daniels explored the right upper mediastinum through a small supraclavicular incision; a slightly enlarged node was found. Biopsy: sarcoid. Two years later, the diffuse lesions had coalesced to massive upper lobe densities. A-G ratio: 4.5:3.05.

Summary: A young white male with transient sarcoidosis of the eyes and chronic lesions of the

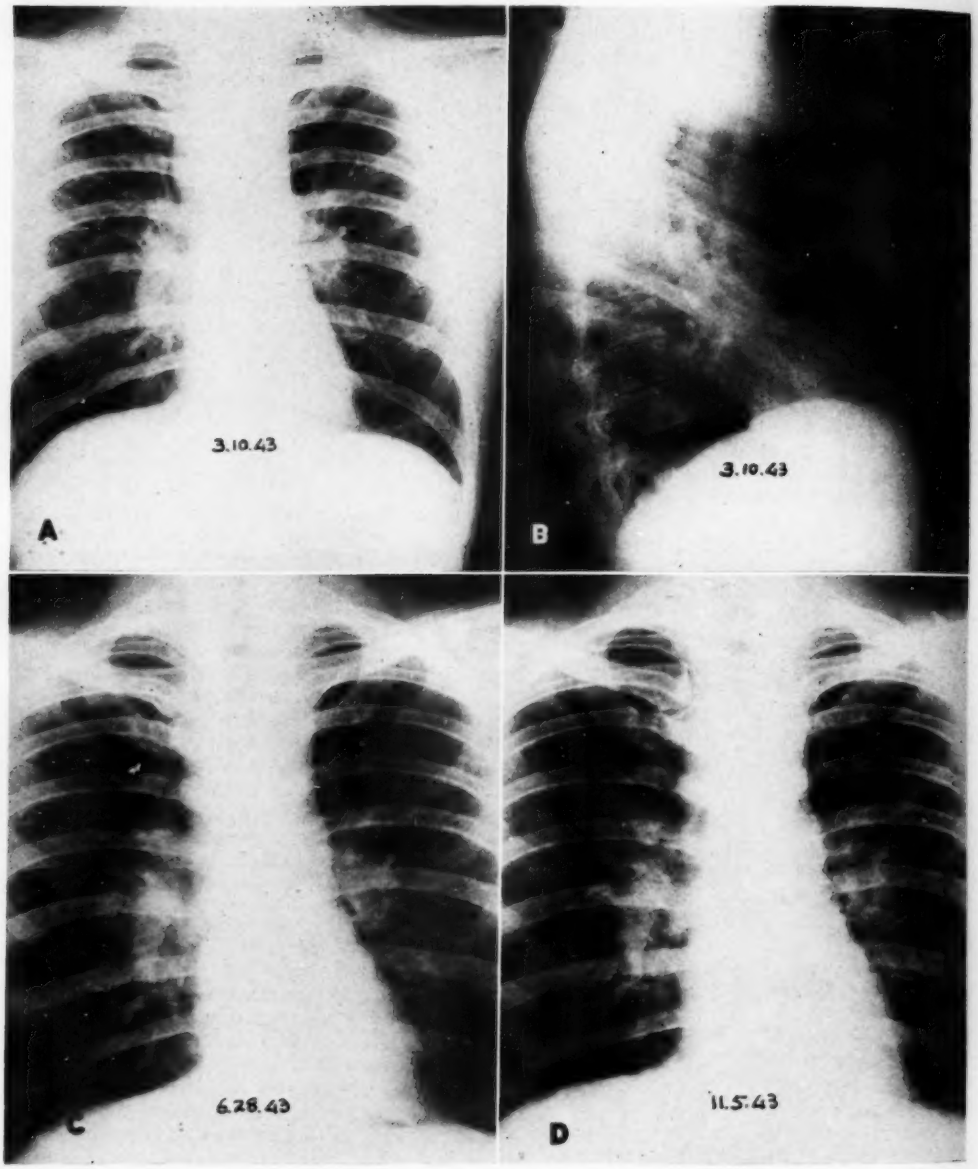


Fig. 4 (A–D). Case 13: Pulmonary sarcoidosis. "Classical" course, first with regression, then with progression and fibrosis. White, male, 28, with iritis, right, chronic. Positive node biopsy. A. Bilateral hilar and right paratracheal adenopathy, with minimal pulmonary infiltrate. B. Lateral view of same. C. Adenopathy diminished; nodular infiltrate extending. D. Slight improvement. See also Fig. 4 (E–H).

lungs repeatedly diagnosed by different physicians as advanced tuberculosis. (Four-year follow-up.)

CASE 14: P. B., white, male, 34. Generalized painless swellings (adenopathy) for three years. Enlarged nodes in neck, axillae, and groins, 1 to 6 cm. in diameter. Roentgen findings: slight hilar and right paratracheal adenopathy. Clinical diagnosis: lymphoblastoma. Biopsy of a cervical and an epitrochlear node: sarcoid. Course: unchanged one month later.

Summary: A white male with peripheral and mediastinal lymph node sarcoidosis.

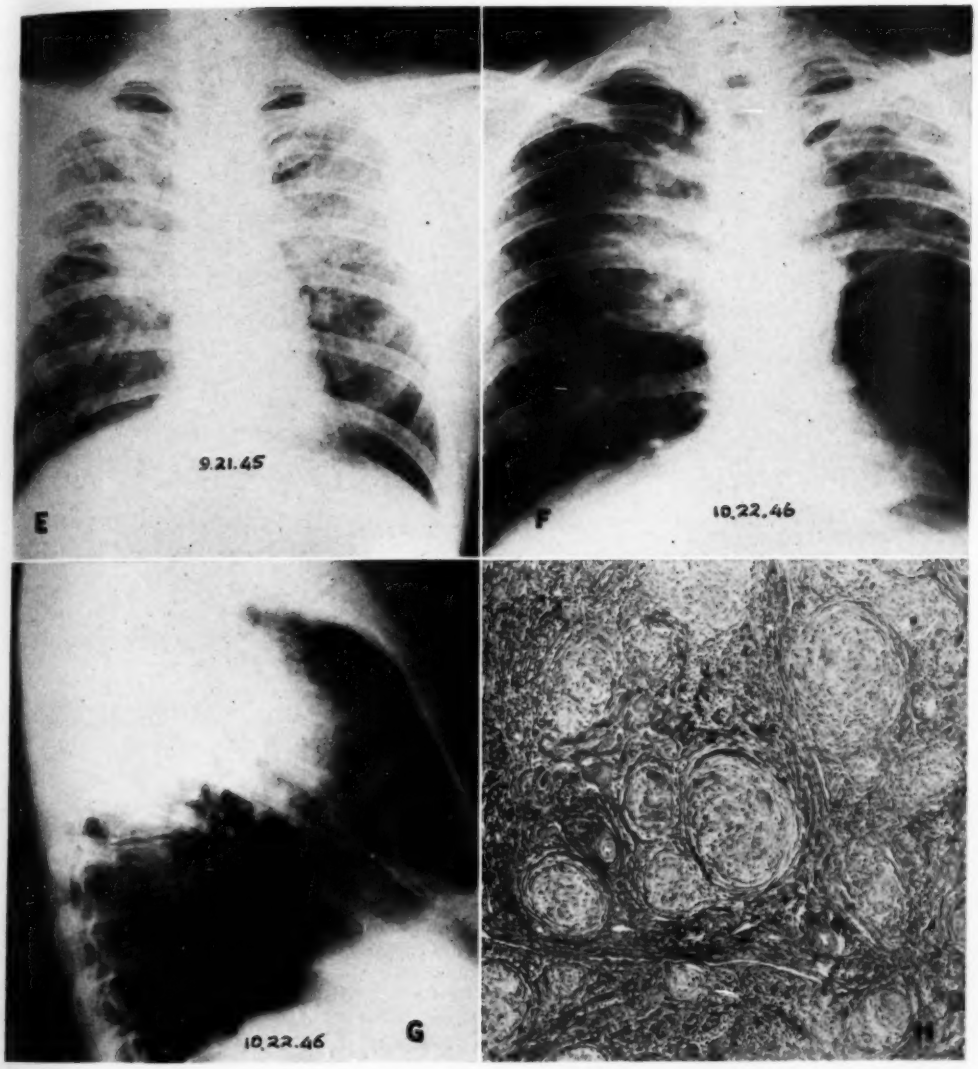


Fig. 4 (E–H). E. Adenopathy apparently gone, but extensive nodular infiltrate in both lungs, especially in the upper halves. F. Coalescent fibrotic and nodular lesions in upper lung fields; mediastinal pleural thickening. G. Lateral view of same. H. Section of node obtained by supraclavicular fossa search, showing multiple discrete non-caseating tubercles and giant cells. (March 1943 to October 1946.)

CASE 15: M. S., colored, female, 23. Small lump in right upper eyelid for four months. Previous cervical lymphadenopathy. Roentgen findings: bilateral hilar and left paratracheal adenopathy; lung parenchyma clear. Clinical diagnosis: granuloma. Biopsy of upper lid nodule: chronic granuloma (sarcoid). Course: sixteen months later improved.

Summary: Puerto Rican female with cutaneous and lymph node sarcoidosis.

CASE 16: E. S., white, female, 29. Right facial palsy, one week. Bilateral parotitis. Left pupil irregular (uveitis). Plasma protein: 6.7 per cent. Roentgen findings: chest negative. Biopsy of parotid swelling: sarcoid. Three weeks later, slight hilar adenopathy. Two months later, slight right paratracheal adenopathy, unchanged after another two months. Two years after the initial examination, chest was again negative.

Summary: White female with multiple system

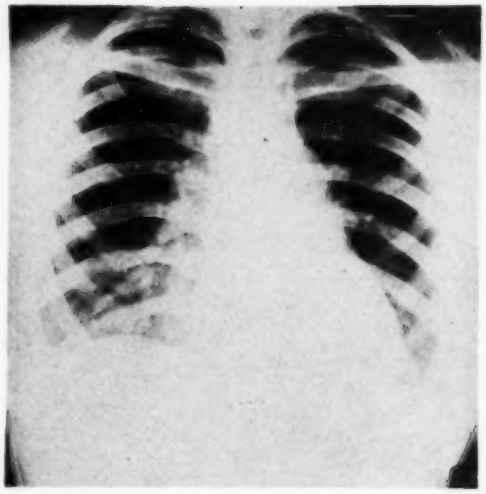


Fig. 5. Case 16: *Early* sarcoidosis (slight hilar and right paratracheal adenopathy). Chest film three weeks previously, negative. White, female, 29, with right facial palsy. Parotid biopsy positive. Subsequent development of right paratracheal adenopathy. Two years later, clear.

sarcoidosis, showing spontaneous improvement. (Two-year follow-up.)

CASE 17: C. J., colored, male, 26. Cough and slight pain in chest for one week. Examination revealed generalized lymphadenopathy; skin rash; enlarged liver. Roentgen findings: bilateral pulmonary infiltrate, "fibrotic" type. Clinical diagnosis: pneumonitis. Biopsy of right epitrochlear node and left forearm skin nodule: sarcoid. A-G ratio inverted. One year later, improved.

Summary: Colored male with generalized sarcoidosis and only slight transient pulmonary symptoms, possibly due to coincidental infection.

CASE 18: M. K., white, female, 56. Abdominal distress after meals, for one year. Subcutaneous nodules on arms and legs; chest pain and sneezing episodes for two weeks. Roentgen findings: bilateral pulmonary infiltration, fibrotic type. Hands: slight cyst-like lesions in four phalanges. Clinical diagnosis: possible gastro-intestinal neoplasm. Biopsy of subcutaneous nodule from left thigh: sarcoid. Three years later, lungs almost clear.

Summary: White female with mild generalized chronic sarcoidosis. (Three-year follow-up.)

CASE 19: J. W., colored, male, 19. Asymptomatic. Small epitrochlear nodes found on routine physical examination; shortly afterwards, axillary nodes palpable; a few skin nodules appeared. Roentgen findings: bilateral hilar and right paratracheal adenopathy; perihilar infiltration. Mantoux, positive. Biopsy of axillary node and skin nodule: sarcoid. Moderate course of radiation to chest (700 r, in air, anterior and posterior fields). No immediate change; lost to present follow-up.

Summary: Young negro with generalized sarcoidosis, apparently early and virtually silent.

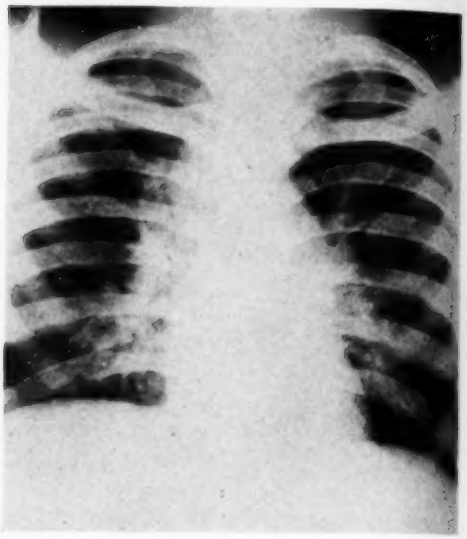


Fig. 6. Case 19: "Sarcoid-type" adenopathy. Bilateral hilar and right paratracheal adenopathy; slight perihilar infiltration. Node and skin biopsy positive. No symptoms.

CASE 20: M. B., colored, male, 23. No symptoms; routine chest x-ray disclosed intrathoracic disease. Following this, physical examination revealed a few small palpable nodes. Roentgen findings: bilateral hilar and right paratracheal adenopathy; nodular pulmonary infiltration. Sputum repeatedly negative for acid-fast bacilli. Biopsy of node: sarcoid. Moderate dose of radiation to chest (800 r, in air, anterior and posterior fields). Six months later, patient much improved.

Summary: Young negro with mild, asymptomatic sarcoidosis, regressing.

CASE 21: M. W., white, male, 24. No symptoms. Routine chest survey. Roentgen findings: bilateral hilar and right paratracheal adenopathy; questionable slight pulmonary infiltrate. Biopsy of posterior cervical node: sarcoid. Small dose of radiation to chest (400 r, in air, anterior and posterior fields). Two months later, no change.

Summary: Silent sarcoidosis, stationary, in young white male.

CASE 22: E. McC., colored, male, 19. Cough for one year; chest pain for one month. Testes sore; left eye red and painful for one month. Parotid glands palpable. Roentgen findings: bilateral hilar and right paratracheal adenopathy; questionable

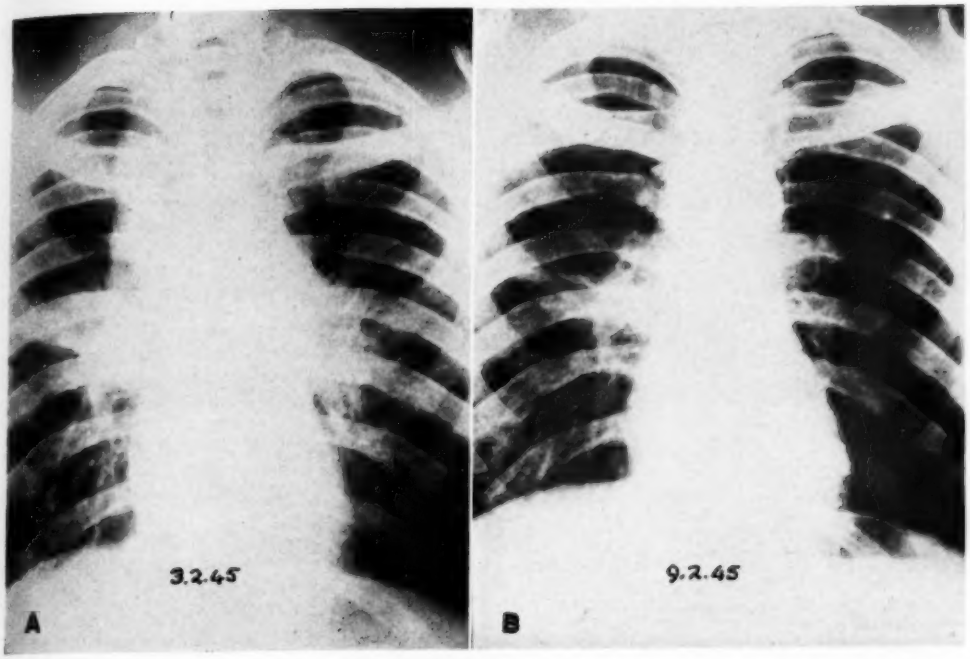


Fig. 7. Case 20: A. Sarcoid-type adenopathy with mediastinal effusion; bilateral pulmonary nodular infiltrate. Node biopsy positive. No symptoms. Case found on routine chest survey. B. Marked improvement approximately six months later.

pulmonary haziness. Hands: coarse phalangeal trabeculations. Clinical diagnosis: possible sarcoidosis. Biopsy of right parotid: sarcoid. Course: slight improvement two months later.

Summary: Young negro with generalized sarcoidosis.

CASE 23: J. H., colored, male, 18. No symptoms. Routine annual chest survey disclosed bilateral hilar and right paratracheal adenopathy, with nodular infiltration of both lungs. Biopsy of node from left supraclavicular fossa: sarcoid. Relatively heavy irradiation of the chest at another hospital (1,100 r, in air, to anterior and posterior fields 15 × 15 cm.). One month later, no change.

Summary: Young negro with extensive, silent intrathoracic sarcoidosis.

CASE 24: J. A., colored, male, 26. Abdominal pains, chronic, intermittent. Nodular eruptions on face, eyelids, elbows, and shins. Corneal opacity, left eye (mild uveitis). Roentgen findings: bilateral hilar and right paratracheal adenopathy. Clinical diagnosis: possible appendicitis. Biopsy of skin nodule and inguinal node: sarcoid. The abdominal pain cleared up spontaneously, but seven months later, the chest findings were unchanged.

Summary: Negro with definite intrathoracic, ocular, and cutaneous sarcoidosis and probable abdominal node sarcoids, with transient symptomatic mesenteric adenitis.

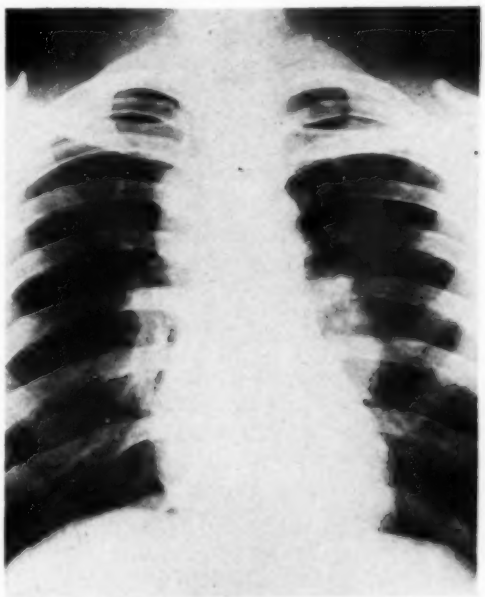


Fig. 8. Case 21: Sarcoid-type adenopathy (hilar and right paratracheal) with questionable slight pulmonary nodulation. Node biopsy positive. No symptoms. Case found on routine survey.

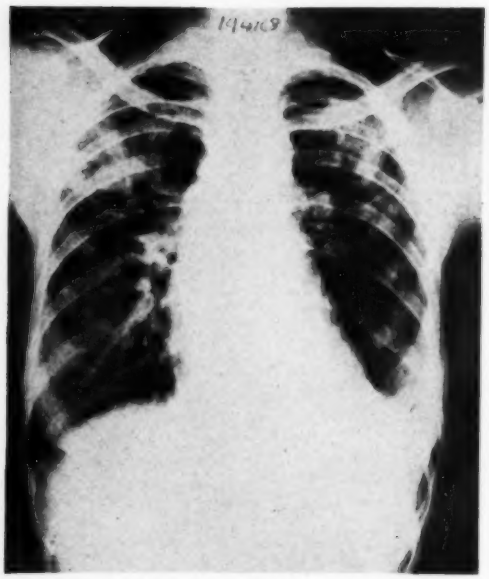


Fig. 9. Case 26: Sarcoidosis. Nodular and coalescent densities in upper two-thirds of each lung; small left basal effusion. Node biopsy positive.

CASE 25: M. B., white, female, 74. Intestinal obstruction. Roentgen findings: slight hilar adenopathy; lungs clear. Obstructive sigmoid lesion. Development of peritonitis and death. Necropsy: carcinoma of sigmoid; hilar adenopathy (microscopically, sarcoidosis).

Summary: An elderly white female with cancer of the colon and, purely incidental, asymptomatic mediastinal node sarcoidosis.

CASE 26: R. J., colored, female, 30. Dysuria and abdominal pain for one month; gonorrheal urethritis. Roentgen findings: patchy densities and nodular lesions in upper two-thirds of each lung. Lymphadenopathy developed on the ward. Biopsy of left epitrochlear node: sarcoid. Three months later, lungs improved; two months later, lungs unchanged; left basal pleural thickening developed.

Summary: Negress with silent pulmonary sarcoidosis; peripheral sarcoid adenitis developing during treatment for gonorrheal salpingitis.

CASE 27: L. B., colored, male, 23. Abdominal pain for two weeks. Cough and slight fever developed while patient was under medical observation. Roentgen findings: bilateral hilar and right paratracheal adenopathy; nodular pulmonary infiltration. Biopsy of node: sarcoid. Moderate radiation to the mediastinum (800 r, in air, anterior and posterior). Six months later, no change.

Summary: Negro with silent pulmonary sarcoidosis and probable symptomatic abdominal node sarcoids.

CASE 28: H. P., white, female, 27. Slight dry cough for four weeks. Routine chest film disclosed extensive nodular infiltration of the entire right lung, and very slight nodulation of the left lung. In view of patient's excellent general status, a roentgen diagnosis of sarcoid was suggested. *Note:* This patient had chest films six months, one year, and three years previously, all reported by competent observer as negative. Hands negative. Biopsy of a small right cervical node: sarcoid. Course unchanged.

Summary: A physician's wife with asymptomatic pulmonary sarcoidosis.

CASE 29: J. D., colored, female, 22. Pain in left costovertebral angle for two weeks; moderate anemia; splenomegaly; scaly lesions on legs. Roentgen findings: bilateral hilar adenopathy with slight pulmonary nodulation. Hands: coarse trabecular pattern in phalanges and metacarpals (questionable sarcoid myelosis). Clinical diagnosis: infarct. Biopsy of skin nodule: sarcoid. One month later, improved.

Summary: Colored female with abdominal (notably splenic), thoracic, and cutaneous sarcoidosis.

CASE 30: H. H., colored, male, 22. No symptoms. Abnormal densities found on routine chest film at separation center. Roentgen findings: bilateral hilar adenopathy; slight pulmonary nodulation. Tuberculin: 1:10,000 positive. Sputum negative. Biopsy of cervical node: sarcoid. Course: not known.

Summary: Silent pulmonary sarcoidosis in young negro.

CASE 31: E. W., white, female, 50. Dyspnea on exertion and precordial pain for one year. Slight splenomegaly. Roentgen findings: bilateral hilar and right paratracheal adenopathy; slight infiltration or lobular atelectasis in middle third of right lung. A-G ratio: 3.71:2.99. Clinical diagnosis: cardiovascular disease. Biopsy of a small right cervical node: sarcoid. Course: no change after one month.

Summary: Middle-aged white female with incidental, silent pulmonary sarcoidosis and possible myocardial sarcoidosis.

CASE 32: M. M., white, female, 24. Pain in abdomen for twelve days. Slightly enlarged liver and spleen. Roentgen findings: diffuse miliary lesions in both lungs. Clinical diagnosis: deferred. Course: some small inguinal nodes developed; one was removed and revealed sarcoid on section. One month later, chest unchanged; patient clinically well. (Case reported by courtesy of Drs. E. E. Simpson and C. E. Grayson, of Sacramento.)

Summary: Young white female with silent pulmonary sarcoidosis and possible abdominal node sarcoids.

CASE 33: I. C., colored, female, 48. Cough and dyspnea for three years. In tuberculosis sanatorium

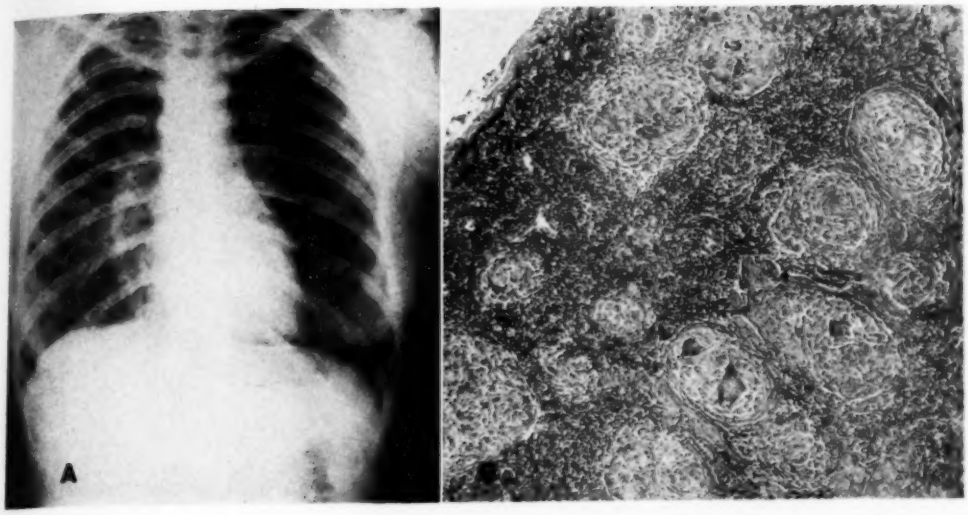


Fig. 10. Case 28: A. *Early* sarcoidosis (disseminated nodular lesions in most of right lung and in parts of left). Chest films made several weeks and months previously negative. White, female, 27, in excellent physical condition, with slight dry cough for four weeks. Node biopsy positive. B. Section from node showing multiple discrete, non-caseating tubercles; no visible asteroid bodies; multiple giant cells.

for eighteen months, with sputum always negative. Recently skin lesions developed over body and extremities, and a few enlarged peripheral nodes. Roentgen findings: bilateral, diffuse nodulofibrotic lesions in lungs, with bullous-like areas in left upper lobe. Clinical diagnosis: tuberculosis or sarcoidosis. Biopsy of node from left axilla and skin from plaque on back: sarcoid. A-G ratio: 3.58:5.42. Eight months later, unchanged.

Summary: Colored female with pulmonary and cutaneous sarcoidosis, chronic.

CASE 34: L. C., white, female, 27. Slight weight loss and asthenia for seven months. Tuberculin test and sputum reported positive on one occasion at a private sanatorium, but negative six times under our observation. Examination of gastric washings negative on three occasions. Coccidioidin test negative. No fever. Reversed A-G ratio. Roentgen findings: bilateral pulmonary infiltration, central three-quarters of each lung; slight right hilar adenopathy. Few small calcific densities in right apex. Biopsy of small right cervical node: inflammatory tissue. Three months later, patient clinically well; roentgen findings unchanged.

Summary: White female with probable chronic pulmonary sarcoidosis, and possible obsolete right apical re-infection type tuberculosis.

CASE 35: D. W., colored, female, 38. "Cold in chest" for two weeks. Slight generalized adenopathy. Slight scarring of some skin areas from "old rash." Roentgen findings: bilateral hilar and right mediastinal adenopathy. Clinical diagnosis: lymphosarcoma. Sternal bone-marrow puncture negative for tumor; not studied for possible sarcoids; specimen unavailable at this time. A-G ratio: 3.58:4.72. All tests for tuberculosis, etc., negative. Final diagnosis after prolonged clinical study, sarcoidosis. Patient lost to follow-up.

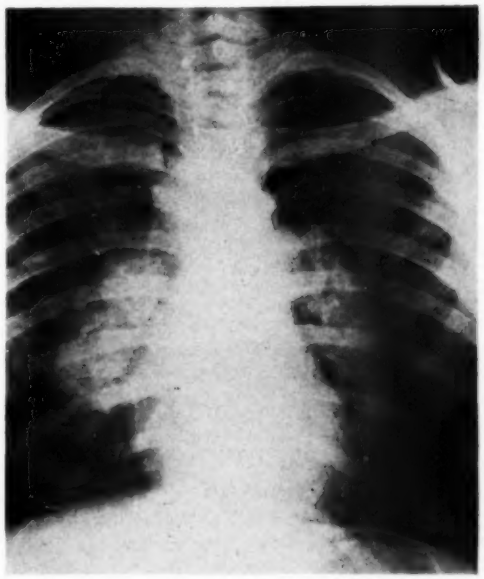


Fig. 11. Case 30: Sarcoidosis; "potato node" type, probably early. Bilateral hilar adenopathy; slight pulmonary nodulation. Node biopsy positive. No symptoms. Case found on routine chest survey.

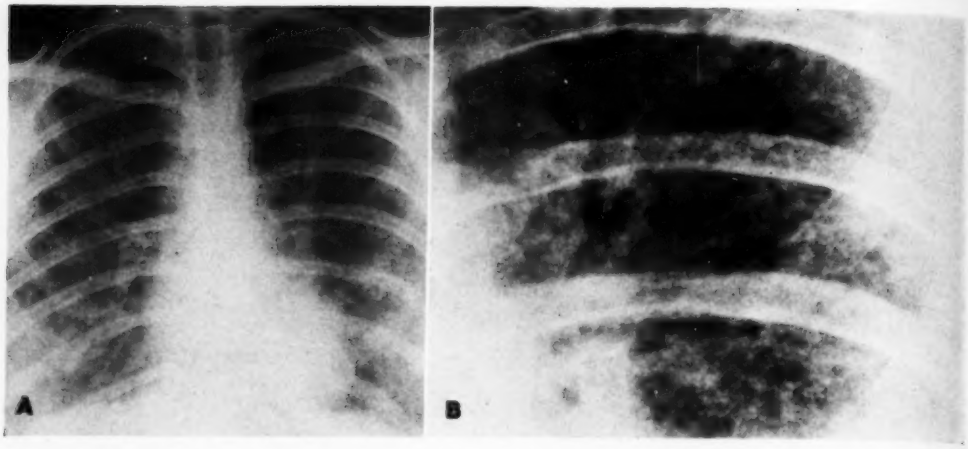


Fig. 12. Case 32: A. Sarcoidosis: miliary type, probably early. Diffuse miliary lesions in both lungs. Node biopsy positive. White, female, 24, with abdominal pain for 12 days. Lung changes found at fluoroscopic examination of the alimentary tract. B. Miliary lesions in left upper lung field.

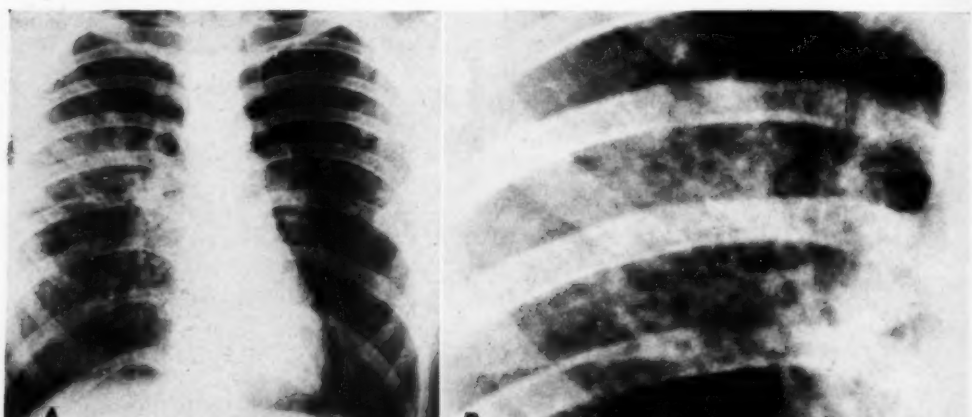


Fig. 13. Case 36. A. Sarcoidosis: nodular type, early. Disseminated nodular lesions in middle two-thirds of each lung. White, female, 23, with transient, mild dysphagia. Lung changes found at fluoroscopic examination of the esophagus. B. Nodular lesions in right upper lung field.

Summary: Colored female with sarcoidosis of the mediastinal nodes and probable old sarcoids of the skin.

CASE 36: L. M., white, female, 23. Slight dysphagia for one week; otherwise perfectly well and active. Roentgen findings: esophagus and stomach negative; disseminated pulmonary nodular lesions, middle two-thirds of each lung. All tests negative. Exploration of right supraclavicular fossa refused. Clinical diagnosis: sarcoidosis. Two months later, patient clinically well, but chest film unchanged.

Summary: White female with pulmonary sarcoidosis, asymptomatic.

SUMMARY

The most frequent type of sarcoidosis encountered clinically is one with hilar lymphadenopathy and pulmonary infiltration. An increasing number of such cases are being discovered in routine chest surveys and are being interpreted as tuberculosis, Hodgkin's disease, mediastinal tumor, and other entities. It is desirable that the possibility of sarcoidosis be kept in mind in such instances, and the attempt

made to establish the correct diagnosis by microscopic examination. "Sarcoidosis should be considered in the differential diagnosis of all cases of chronic painless lymphadenopathy, whether there are demonstrable lesions of the skin, bones and lungs or not. The diagnosis is not established by pathological examination alone, but only in conjunction with the appropriate clinical and bacteriological evidence to eliminate other granulomatous infections." (5)

A palpable lymph node or skin nodule is the most desirable tissue for microscopic examination. However, when *none* such is evident, exploration of the mesial end of the right supraclavicular fossa through a short incision will frequently yield *an upper anterior mediastinal node* for study and positive diagnosis.[3]

In the absence of microscopic evidence of non-caseating tubercles, there are certain roentgen findings suggestive, but not pathognomonic, of the disease. These include extensive bilateral nodular parenchymal densities in persons having no symptoms of disease, and especially the combination of nodular densities with bilateral hilar and right paratracheal adenopathy. Grossly enlarged hilar nodes alone, in an apparently healthy person, are also a highly suggestive sign.

Absence of pulmonary involvement at one stage of sarcoidosis is no assurance it will not be silently present months or years later. The course of a given case is usually quite unpredictable. The lesions may regress, remain stationary, or progress without apparent reason. This renders estimation of the beneficial effects of therapy, such as roentgen irradiation, extremely difficult. Some cases progress to diffuse, coalescent pulmonary fibrosis, with variable degrees of cardiac embarrassment. Only one of our cases appeared to show such a complication. In some, coincidental tuberculosis develops; one of our patients has calcified lesions in one pulmonary apex (pre-existing obsolete tuberculosis?); none has developed frank phthisis to date. Cerebral, meningeal, or cardiac involvement may lead to a fatal outcome. This could not be proved in any of our cases.

[3] Daniels, A. J., and Wilbur, D. L. To be published.

CONCLUSIONS

The *early* roentgen finding in pulmonary sarcoidosis may be one of four types:

1. Disseminated miliary parenchymal lesions,
2. Diffuse or localized nodular parenchymal lesions,
3. Parenchymal densities with hilar and paratracheal adenopathy,
4. Hilar and paratracheal adenopathy alone.

This adenopathy is present in about two-thirds of the early cases, and is usually of a pattern we have designated "sarcoid-type," consisting of bilateral hilar and right paratracheal lymph node enlargement.

The miliary type of pulmonary sarcoidosis occurred as an early finding in a minority of our cases.

ACKNOWLEDGMENT: The writer is indebted to Dr. B. R. Kennedy for invaluable assistance in compiling the data on many of the cases reported in this paper; to Dr. R. R. Newell for permission to review the films of eleven cases from the Stanford University Hospital x-ray files; to Dr. R. S. Stone for similar permission in connection with four cases from the University of California Hospital x-ray files; to Drs. S. F. Thomas and C. L. Boice for assistance in locating some of the cases seen while they and the author were on duty at the U. S. Naval Hospital, Oakland, Calif., and, finally, to the many physicians who aided with clinical and other data on the cases under review.

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DISCUSSION OF SYMPOSIUM ON DISEASES OF THE CHEST

(Papers by Wm. Dock, Horace W. Jamison and Ray A. Carter, and L. Henry Garland)

Leo G. Rigler, M.D. (Minneapolis, Minn.): Dr. Dock's very interesting paper was most satisfying to me, since I am one of those "old-fashioned" people who have been trying to oppose the trend to treat minimal tuberculosis rather casually and who still believe in complete bed rest for the earliest tuberculous lesion. Dr. Dock's theory, of course, tends to push us in that direction. As he himself said, however, the experimental proof of his theory is still to be obtained, although he has built up a very satisfactory, logical type of case.

I think it should be said that pressures in the pulmonary circulation are subject to considerable differences and that one cannot make inferences or transfer observations from the peripheral circulation or from other data, since there are apparently a lot of compensatory mechanisms in the pulmonary circulation of which we understand very little. For instance, if you have an arteriovenous fistula of the peripheral circulation, you will get a prompt increase in the size of the heart. If you have an aneurysm or fistula in the pulmonary circulation, apparently nothing happens to the heart; some sort of compensatory mechanism is in evidence. So that it is necessary to prove unequivocally these changes in pressure, although the case certainly has a most logical and attractive sound.

We know very little about coccidioidomycosis in Minnesota. Fortunately it has not yet invaded us except by way of information which we get from our staff who were incarcerated in sunny and dusty California during the war and brought back a lot of data about it. I'm afraid I cannot comment adequately upon it.

Dr. Garland's presentation on the problem of sarcoidosis, while illuminating and comprehensive, was disappointing. When I saw the title I was confident that an investigator of our Chairman's talents would surely give us the answer to the problems in the early diagnosis and differentiation of sarcoidosis Unfortunately, Dr. Garland has no magic formula, although he has beautifully oriented and clearly enunciated the picture of the findings.

His conclusions differ in no respect from those that we have come to from our experience. I should like to add a word to his criteria in the typical case—that is, a bilateral hilar adenopathy and a right paratracheal lymph node enlargement—so that it becomes *symmetrical* bilateral hilar adenopathy, because I think, in the classical cases he showed, symmetry is a very striking thing. I would like to ask Dr. Garland if he has had any experience with the skin test for sarcoidosis made by grinding up a lymph node and also whether he has any information with regard to the more recent bacteriological studies of such lymph nodes.

W. Edward Chamberlain, M.D. (Philadelphia): I was fascinated by Dr. Dock's presentation. He very modestly calls it speculative, but I would say that, while the evidence is circumstantial, circumstantial evidence can sometimes be quite devastating. I find his ideas extremely stimulating and exciting.

Dr. Garland, I believe, made a point that I would like to emphasize—that when we begin to x-ray large numbers of apparently healthy persons, we begin to have a better understanding of sarcoidosis, or at least to find out something about it. Before we began to do mass surveys or to examine large numbers of men on induction or release from active military or naval service, we had an erroneous impression of the symptomatology of sarcoidosis because we saw only the sick individuals. There has been a particularly high incidence of the big "potato nodes" mentioned by Dr. Garland in these mass surveys. Planigraphic studies in such cases reveal something very interesting, namely, a complete absence of narrowing of the bronchial airway through

the massive node. And that, of course, provides us with a very striking differential feature from neoplastic masses of similar size. I must say that we feel justified in going pretty far toward a definite diagnosis of sarcoidosis when we find this complete absence of narrowing of the airways in these nodes.

In connection with Dr. Jamison's paper, I recalled a rather astonishing case of laboratory infection which came to the attention of Dr. Dock, Dr. Garland, Dr. Newell, and myself back in 1932 or 1933. One of our medical students, playing around with an old dry culture of *Coccidioides immitis*, looked up and saw some fuzz floating in the air in front of him. Frightened, he closed the test tube and forgot about it. A couple of weeks later he complained of a chest condition which looked like tuberculosis and which Dr. Newell and I thought was tuberculosis. Subsequently an erythema nodosum appeared and a little later a pure culture of *Coccidioides immitis* was obtained from the young man's sputum. In those days we had no knowledge of the nature of valley fever or of any form of coccidioidomycosis which was not fatal, and we waited for our student to die. He surprised us all by promptly getting well, and a few years later, when we discovered the bacteriological basis for valley fever, we were able to understand his beautiful recovery much better than was possible at the time.

George M. Wyatt, M.D. (Washington, D. C.): I plan to limit my discussion largely to sarcoidosis but I should first like to state that coccidioidomycosis is a real diagnostic problem for those of us in the East, where it is seen so rarely that it is difficult to keep it in mind as a possibility. We had one patient who had never been in California but contracted coccidioidomycosis while cleaning an airplane which had recently come from that state.

In regard to sarcoid, it is my belief that the most significant and diagnostic single finding, and the one which has been heavily emphasized by Dr. Rigler, is the bilateral symmetry of the lymph node enlargement. If measurements are made from the midline, you will find that the nodes extend equal distances from the midline almost to the millimeter. The right paratracheal nodes, of course, show enlargement without corresponding enlargement of the left because they are the only unpaired lymph nodes in the chest. In a recent conversation, Dr. Harry Hauser informed me that he had also encountered the symmetrical enlargement quite constantly.

I saw approximately 150 cases of sarcoid while at the Walter Reed Hospital in Washington. Because that hospital was a tumor center, many of these patients came with a diagnosis of lymphoma. Our impression, therefore, of the more common change was that of lymphadenopathy. In our experience, bone involvement was extremely rare. Only one patient had any demonstrable bone lesions, although a search for these was made in every case. We did not recognize osteoporosis in any of these patients.

Erythema nodosum is either the same disease as sarcoid, or the chest manifestations of the two diseases are exactly alike, for the roentgenogram permits no differentiation between the two. Miliary sarcoid may exactly simulate miliary tuberculosis, but the patient with miliary tuberculosis does not usually walk into the office; he is carried in.

There is one question that I should like to ask Dr. Garland: Should we call the lesions he has demonstrated early or minimal? We have seen some cases in which there was first adenopathy which receded with the appearance of miliary lesions in the lung parenchyma. Then the miliary lesions receded and the lymph nodes again enlarged. When you have that "coming" and "going," it is somewhat difficult to tell what is coming and what is going.

R. R. Newell, M.D. (San Francisco): Dr. Jamison and Dr. Carter have had an extraordinary opportunity for a broad experience with coccidioidal infection in this geographically limited disease. Dr. Jamison stressed the variation in the roentgen appearance of coccidioidal infection in the lung and then he showed us several cases with quite typical appearance, imitating virus fever. I have seen this disease imitate bronchopneumonia, Friedländer's pneumonia, and even metastatic cancer. We had one case which developed an appearance of miliary tuberculosis that cleared up in the course of a few weeks; so that one realized that it was not a generalized miliary spread of the disease but was merely many small coccidioidal tubercles within the lung. We classified this case as primary, for it did not go on to the grave granulomatous phase.

The development of these solitary granulomas, these round spots, is very interesting and happens much more often in coccidioidal infection than it does in tuberculosis. They resemble what we have been calling, in tuberculosis, nummular tuberculosis or Assmann foci. I was glad to see Dr. Jamison classify them as primary. They are granulomas, to be sure, but when one says "coccidioidal granuloma," he ordinarily means the stage of the disease with metastatic granulomatous lesions, the stage which shows a mortality of 50 per cent, a very different matter from the primary stage, which is so very usually benign, as these nummular lesions are benign.

In one case of primary coccidioidal infection, we have watched the development of a solid lesion in the lower lobe which has remained practically unchanged in roentgen appearance for over three years.

Dr. Garland (*closing*): In reply to Dr. Rigler's question, Dr. Carnes at Stanford has performed many skin tests on patients, and made bacteriological studies on removed lymph nodes, but without

conclusive results to date; we still don't know whether or not the disease is due to a virus.

In reply to Dr. Chamberlain, one of Dr. Snapper's original cases and one of ours were diagnosed bronchogenic carcinoma at the initial examination. The enlarged hilar nodes do sometimes cause atelectasis, although I quite agree that this is exceptional.

In reply to Dr. Wyatt, it is possible that a preferential title would have been "minimal" rather than "early." However, some of the cases which we saw were, in our opinion, unquestionably *early;* most may have been minimal. I cannot agree as to the symmetrical nature of the hilar adenopathy; it was seldom truly symmetrical in our cases. Nevertheless, the large number of cases which Dr. Wyatt saw at Walter Reed Hospital entitle him to a "senior" view on this point! I suspect that bone lesions in sarcoid are like the nodal ones; you've got to catch them when they happen to be evident. They may be present for one six-month period and then not demonstrable for months or years, only to reappear later. In our experience, the diffuse, faint porotic type of change is commoner in the phalanges than the classical cystic form.

Roentgen Therapy in Hodgkin's Disease[1]

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THE RAPID response of the lymphoblastoma group to x-ray therapy has been well known for many years. Since the lesions originate in lymphoid cells, which are the most sensitive of all body cells to roentgen rays, lymphoblastomas themselves are also very sensitive (1).

Certain radiologists would treat these lesions with very light dosages because they are impressed by the good temporary response. Others would give intensive treatment, approaching dosages used for carcinoma. It is likely that the most satisfactory response is obtained somewhere between the two extremes.

The method of treatment which has been used at our clinic produces results which, when analyzed, compare very favorably with others so far published. It is our purpose to present statistical data obtained from our records which will give a fairly accurate idea concerning the effectiveness of this method.

A series of 185 cases proved by biopsy will be presented. The biopsy specimens were examined by the Department of Pathology, under the supervision of Dr. E. T. Bell. Another group of 53 cases has been analyzed, in which biopsy specimens were examined elsewhere and considered to show the features of Hodgkin's disease. The slides, however, were not available for confirmation. Clinically the lesions in this group strongly indicated the presence of Hodgkin's disease, although we cannot claim them as proved cases. All cases treated in this department from 1926 through 1942 are included and have been followed to the end of December 1945.

HISTORY

The most commonly recognized of the lymphoblastoma group, Hodgkin's disease, took its name from the man who first recognized it in 1832 as a clinical entity, Sir Thomas Hodgkin (2). Seven cases of lymphadenopathy, accompanied by anemia and splenomegaly followed by cachexia and death, were described by him. He felt that the disease was a primary affection of the lymph nodes rather than some secondary infection. Most of the cases described by Hodgkin are now believed to have been tuberculosis or neoplasm, but at least 2 were true examples of what we recognize as Hodgkin's disease. Tissues from one of these cases are still preserved in the museum of Guy's Hospital and have been proved by Herbert Fox (3), with modern microscopic technic, to have the characteristic histologic structure.

In 1856 Sir Samuel Wilks (4) added to the original description of Hodgkin and pointed out the frequent involvement of liver, kidneys, and lungs. He clearly distinguished Hodgkin's disease from the leukemias. No detailed description of the microscopic pathology was given until Greenfield (5) referred to the chronic inflammation, marked increase in fibrous stroma, and large number of multinucleated cells.

Goldmann (6), in 1892, pointed out the importance of eosinophils, and in 1898 Sternberg (7) described the characteristic giant cells and areas of necrosis. Reed (8), in 1902, correlated the pathological findings with the clinical histories. She gave a more accurate description of the cells than Sternberg and recognized their importance in the diagnosis. The following conclusions were reached by her after extensive studies:

1. We should limit the term Hodgkin's disease to the designation of a clinical and pathological entity, the main features of which are painless pro-

[1] From the Department of Radiology and Physical Therapy of the University of Minnesota and the University Hospitals, Minneapolis, Minn. Accepted for publication in July 1946.

gressive glandular enlargement, usually starting in the cervical regions without the blood changes of leukemia.

2. The growth presents a specific histologic picture, not a simple hyperplasia but changes suggesting a chronic inflammatory process.

3. The microscopic examination is sufficient for a diagnosis. An inoculation may confirm the diagnosis by its negative results [written when the tuberculous nature of the disease was upheld by many].

4. Eosinophils are usually present in great numbers in such growths but not invariably. Their presence strengthens the diagnosis.

5. The causative agent is as yet undiscovered. Tuberculosis has no direct relationship to the subject.

Wallhauser (9) found about fifty synonyms for Hodgkin's disease, demonstrating the confusion regarding classification and etiology. In Germany, the usual designation has been lymphogranuloma. This term is undesirable until more is known about the true nature of the disease. It is also confusing, since there are other types of lymphogranuloma, such as mycosis fungoides, Kaposi sarcoma, Boeck's sarcoid, etc. In America, the term malignant has been added to differentiate it from the other lymphogranulomas, on the assumption that the disease is neoplastic. Mallory (10), one of the principal advocates of the neoplastic nature of Hodgkin's disease, calls it "lymphoblastoma." Other terms used on occasion are "malignant lymphoma," "megakaryoblastoma," lymphoma, and lymphadenoma. The last term seems to be favored by the British. (These names are, however, used in a wider sense and include other entities.)

To avoid confusion, the term "Hodgkin's disease" is by far the most desirable, since it preserves the condition as a distinct entity apart from the other members of the same large group. Krumbhaar (11) advocates the designation "lymphomatoid diseases" in reference to the leukemias, lymphosarcoma, agranulocytosis, erythroblastosis, and other similar conditions.

ETIOLOGY

1. *Tubercle Bacillus:* Most of the early authors were convinced that the tubercle bacillus was responsible for the production of Hodgkin's disease. In 8 of Sternberg's original 13 cases definite tuberculosis developed. More recent authors deny vigorously the etiologic importance of the tubercle bacillus. They believe it to be a coincident or secondary invader. Its occurrence is quite frequent, some authors placing its incidence as high as 20 per cent (12). It is logical to suppose that old tuberculous lesions may become reactivated or new infections occur due to the weak, cachectic state of patients suffering from Hodgkin's disease.

2. *Diphtheroid bacilli* are also thought by some authors to be factors in the etiology of the disease, Bunting and Yates (13) and de Negri and Mieremet (14) being among the most ardent advocates of this theory. Bunting and Yates named the organism *Bacterium hodgkini* and claimed that extracts injected into animals produced Hodgkin's granuloma. Diphtheroid bacilli, as well as other organisms, are found in lymph nodes due to a variety of conditions. They may be air-borne laboratory contaminants (Wallhauser, 9).

3. *Brucella:* Parsons and Poston (15) and Wise and Poston (16) reported positive cultures for organisms in the *Brucella* group in 14 cases of Hodgkin's disease. Cultures from 67 cases of diseases of the lymph nodes other than Hodgkin's disease yielded negative results except in a single instance. No other investigators have been able to confirm these findings.

4. *Filterable Virus:* Twort (17) presented a theory advocating a filterable virus as the etiologic factor, on the basis of a study of allied disorders, such as leukemia of fowls and pernicious anemia of horses. Gordon (18) injected material from Hodgkin's nodes intracerebrally in animals and produced paralysis and death. He concluded that a filterable virus was the causative agent. Negative results were obtained with extracts from nodes involved by carcinoma, sarcoma, etc.

Turner, Jackson, and Parker (19) demonstrated to their satisfaction that the Gordon test was entirely dependent on the presence of eosinophils and was not spe-

cific for Hodgkin's disease. Steiner (20), however, believed the test to be confirmatory if accompanied by histologic examination. He admitted that positive results are occasionally obtained from nodes involved by lesions other than Hodgkin's disease but did not agree that eosinophils are the positive factor.

5. *Neoplastic Theory:* Most modern investigators, including Warthin (21), Mallory (10), and Bell (22), believe Hodgkin's disease to be neoplastic in origin. The high fatality rate and the demonstration of cases in which there is a delayed interval between the so-called primary lesions and metastatic lesions are somewhat convincing. The absence of any proved infectious agent leads one to believe more strongly in the neoplastic theory.

SYMPTOMS AND PHYSICAL FINDINGS

The symptoms of Hodgkin's disease are variable, depending on the stage of progression at the time of the patient's first visit to the doctor. The only complaint may be palpable cervical or axillary lymph nodes. There may be systemic symptoms of greater or less degree, such as fever, weakness, anorexia, and loss of weight. Frequent coincident infections occur, such as tonsillitis, upper respiratory infections, otitis media, and oral infections. These may produce adverse effects.

Weakness is not infrequently the first symptom and in the absence of obvious lymphadenopathy may be very difficult to evaluate. A careful search should be made for enlarged lymph nodes and abdominal masses. An x-ray film of the chest may show lesions characteristic of the disease.

A dry, hacking cough is often the first indication of involvement of mediastinal nodes. Dyspnea, cyanosis, and dysphagia occur later and indicate obstruction due to mediastinal enlargement or to extension of lesions into the lung parenchyma. Pulmonary involvement is often accompanied by fever. Venous engorgement may also occur and is a very distressing symptom.

Nausea and vomiting do not necessarily suggest occurrence of the disease in the gastro-intestinal tract but can best be explained by the systemic effects. Abdominal pain is usually an indication of the presence of enlarged abdominal nodes with pressure effects. The hemorrhagic diathesis present in the disease may produce melena and hematemesis.

Occasionally, paralysis of one or both lower extremities occurs as a result of vertebral or extradural involvement. Collapse of the vertebrae, however, may occur without paralysis. Enlarged retroperitoneal nodes are the commonest cause of backache. This symptom is a sufficient indication for x-ray therapy to the retroperitoneal region in the presence of Hodgkin's disease, even in the absence of other positive signs.

Pain usually occurs in bone lesions before these are actually demonstrable on the x-ray film. In 13 cases reported by Jackson and Parker (23), pain was present for two to twelve months before positive roentgenograms were obtained, in spite of repeated examinations. Conversely, large bone lesions have been found without symptoms.

Pruritus often occurs early in the disease, and its presence is disturbing. It can be severe enough to lead to marked excoriations of the skin from scratching. Often there is no visible change but on microscopic examination, many of these cases will show some degree of lymphocytic infiltration. The more specific lesions have been designated "lymphogranulomatosis cutis" and have a nodular or ulcerated appearance. Pruritus is occasionally the first symptom, and any case of idiopathic pruritus should be examined closely for evidence of enlarged lymph nodes.

PATHOLOGY

According to Bell (22), the lymph nodes on gross examination are enlarged, pale, and firm, and of fleshy or fibrous consistence. They have a definite tendency to remain discrete and seldom become matted together. The same appearance is seen on gross examination in aleukemia and lym-

phosarcoma. On section, areas of caseous necrosis are rather common in the lesions of Hodgkin's disease. This finding has been responsible for the suggestion of a tuberculous etiology, but the necrosis is actually due to the disease itself.

The microscopic structure is widely variable in different cases and to a lesser extent in various lymph nodes from the same individual. Some structural differences occur, also, related to the stage of the disease. There are certain features, however, distinctive of Hodgkin's disease, as an increase in the number and size of the reticulum cells, often with the formation of giant cells of Dorothy Reed type; increase of reticulum fibers with the formation of areas of fibrosis; obliteration of the sinusoids; eosinophil cells; areas of necrosis and increase of lymphoid cells.

Jackson and Parker (24) would restrict the diagnosis of Hodgkin's disease to cases showing Dorothy Reed cells. Bersack (25) states that the Reed cells are present only in the later course of the disease. In many of his cases, even after careful examination, Dorothy Reed cells were not found, but specimens from the same patients, after further progression of the disease, showed typical findings.

Enlargement of the lymph nodes with obliteration of the sinusoids is of great diagnostic importance. The areas of necrosis can be distinguished from tuberculosis by their sharp demarcation from the surrounding tissue and the absence of epithelioid cells. Often there are large numbers of eosinophil leukocytes in the cellular areas.

The cellular forms of Hodgkin's disease blend with leukemia. There is also a blending with lymphosarcoma and leukemic reticuloendotheliosis. A single node is often insufficient for differentiation, and difficulties are encountered even at autopsy. Occasionally one of the lesions of Hodgkin's disease grows rapidly and exhibits the histologic structure of a sarcoma.

Jackson and Parker (24) present a new concept of the disease. They describe three types, each of which has a distinct appearance pathologically and a different prognosis. According to these authors, the *paragranuloma* is the early variety, and its main feature is lymphoid hyperplasia, the principal cell being the adult lymphocyte. Reed-Sternberg cells are present in small numbers. The paragranuloma is considered rather benign, but it may progress to the next type, called Hodgkin's granuloma. In the *granuloma* group, the distinguishing features are eosinophilia, necrosis, and fibrosis. This is the group most commonly seen in clinical practice and presents a serious prognosis. The third type, *Hodgkin's sarcoma*, is highly malignant. The principal features are the presence of large tumor cells and Reed-Sternberg cells with only occasional necrosis and relative rarity of the characteristic cells in granuloma. This form is rapidly progressive and fatal in a short time. It is most commonly primary in the retroperitoneal lymph nodes and gastro-intestinal tract but rather uncommon in the peripheral nodes.

Jackson and Parker attach great significance to the histologic appearance as an indication of the prognosis of the disease. Among the numerous authors who dispute this are Slaughter and Craver (26), who reported 14 cases of Hodgkin's sarcoma, with 5 patients surviving over three years, 3 of these for more than five years, and one for over seven years—a good survival rate for any group of Hodgkin's disease. The patients in their general series who survived less than six months presented no consistent histologic picture.

DIAGNOSIS

1. A positive diagnosis of Hodgkin's disease depends entirely on its histologic appearance. Any lymph node which is definitely enlarged can be selected for biopsy, but the largest is probably the best choice, since sections can be made from more widely separated areas.

2. In a smaller percentage of cases no enlarged lymph node can be palpated and onset may be in the mediastinal nodes or abdominal nodes. In the mediastinal cases, examination by means of x-ray will

TABLE I: SEX INCIDENCE OF HODGKIN'S DISEASE
(185 Cases with Positive Biopsy)

Males	115 (62%)
Females	70 (38%)
TOTAL	185 (100%)

be of great assistance in determining the site and extent of the lesion. In these cases a tentative diagnosis of lymphoblastoma can be made, with the aid of the history, physical examination, and laboratory studies, but it may be impossible to determine the subdivision. X-ray therapy should be suggested as a therapeutic test to determine response, which occurs quite rapidly in lymphoblastomas.

3. Certain of the clinical findings commonly found in Hodgkin's disease, such as pruritus, Pel-Ebstein fever, and lymph node enlargement, should lead to a strong suspicion of the diagnosis. Eosinophilia is suggestive for differentiation from diseases not having this finding.

DIFFERENTIAL DIAGNOSIS

It is sometimes difficult to differentiate Hodgkin's disease from the other members of the lymphoblastoma group even when a biopsy has been obtained, *viz.*, the leukemias and lymphosarcomas. Metastatic carcinoma is often difficult to differentiate from Hodgkin's sarcoma. Tuberculous adenitis also provides considerable trouble because of the necrosis, fibrosis, and the similarity of the constituent cells. Other types of lymphadenopathy accompanying local or generalized inflammatory disease are less confusing clinically and microscopically.

When an enlarged spleen is the outstanding feature, the diagnosis may be obscure. Other commonly recognized types of splenomegaly are those of Banti's syndrome, splenic anemia, Gaucher's disease, thrombocytopenic purpura, amyloid disease, syphilis, malaria, the leukemias, etc. In many cases, the diagnosis is obvious from other clinical and laboratory findings, but biopsy is necessary for confirmation.

In cases with bone involvement, the appearance may simulate multiple myeloma. The characteristic Bence-Jones protein, elevated globulin, and diagnostic bone marrow studies are conclusive in myeloma.

INCIDENCE

Race: Hodgkin's disease attacks individuals of every race without discrimination. In America, it affects Negroes and whites to about the same extent.

Sex: The disease is more prevalent among men than in women. Of Wallhauser's (9) series of 1,447 cases collected from the literature, about 70 per cent occurred in males. In our series of 185 patients with proved Hodgkin's disease (Table I) 62 per cent were men and 38 per cent females.

TABLE II: AGE DISTRIBUTION OF HODGKIN'S DISEASE
(185 Cases with Positive Biopsy)

	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80	81–90
Number	6	23	50	29	30	24	16	6	1
Per cent of total in each decade	3	12	27	16	16	13	9	3	1
Duration of life in months from first treatment for each decade	37	53	33	45	43	16	19	17	1

Average survival time for 185 cases from first treatment at University of Minnesota Hospitals: 33.0 months (25 patients still living).
Average interval from time of onset to first treatment: 16 months (171 cases).
Median age: 34 years. Average age: 38 years.

Age: In most series reported, the onset in the greatest number of cases occurred in the third decade of life. In our series, as shown in Table II, the greatest percentage were in the third decade, 27 per cent as compared with 12 per cent in the second decade and 16 per cent in the fourth decade; extremes of age were 5 and 81 years, and the average age was 38 years. (The age as given in this series is the age at time of treatment.)

SITE OF ONSET

As in other series, most of our cases of Hodgkin's disease seemed to originate in the peripheral lymph nodes (Table III). The disease began in the cervical nodes in 61 per cent of the series, in the axillary nodes in 10 per cent. Some of the more unusual sites of origin were the breast, thyroid, and tonsil, each represented by one case; the bone, 3 cases; the skin 9 cases. The last figure includes those cases in which pruritus was the first symptom noted. Many cases which have their origin in deeper areas, such as the abdomen, are not discovered until peripheral node involvement has occurred, and are then mistakenly thought to have begun in these peripheral areas.

TABLE III: SITE OF INITIAL INVOLVEMENT IN HODGKIN'S DISEASE

(185 Cases with Positive Biopsy)

	Cases	
Cervical lymph nodes	112	(61%)
Axillary lymph nodes	19	(10%)
Supraclavicular lymph nodes	4	(2%)
Inguinal lymph nodes	8	(4%)
Mediastinum	11	(6%)
Mediastinum plus pulmonary infiltration	3	(2%)
Abdominal nodes	7	(4%)
Skin	9	(5%)
Bone	3	(2%)
Breast	1	(0.5%)
Generalized	6	(3%)
Thyroid	1	(0.5%)
Tonsil	1	(0.5%)
TOTAL	185	(100%)

SITE OF INVOLVEMENT

Since Hodgkin's disease is histologically a disease of the reticulo-endothelial system, it may be found in almost any organ of the body. The peripheral lymph nodes are the most frequently involved. In our series (Table IV) 98 per cent of the cases showed some type of peripheral lymphadenopathy at some time in the course of the disease. The cervical nodes were involved in 83 per cent of the cases, followed by the axillary nodes in 65 per cent, inguinal in 44 per cent, and supraclavicular in 21 per cent.

In Craver's series (27) of 220 cases, lesions of the lung were present in 29 per cent of the total number. In our series of 185 proved cases, intrathoracic lesions were present in 66 per cent, which appears to be higher than in most comparable groups. Mediastinal lesions were present in 61 per cent of the total number and parenchymal lesions in 30 per cent. In all these cases the involvement was verified either by chest roentgenograms or at autopsy. Pleural effusions were present in 10 per cent of the cases, which is somewhat less than in most other groups. In Wright's series (28) of 60 intrathoracic cases, x-ray examination showed involvement of the mediastinal nodes in 57 patients. Twenty-one patients had parenchymal lesions and there were 17 instances of pleural effusion.

TABLE IV: SITE OF INVOLVEMENT IN HODGKIN'S DISEASE

(185 Cases with Positive Biopsy)

	Cases	Per Cent
Peripheral lymph nodes	181	98
Cervical	154	83
Axillary	120	65
Supraclavicular	38	21
Inguinal	81	44
Thoracic	123	66
Mediastinal lymph nodes	113	61
Parenchymal involvement	56	30
Pleural effusion	18	10
Abdominal lymph nodes (plus retroperitoneal)	100	54
Spleen	57	31
Skin	31	17
Bone	37	20
Nervous system	4	2
Muscle	8	4
Liver	19	10
Omentum	1	0.5
Parotid gland	1	0.5
Pancreas	5	3
Stomach	6	3
Adrenals	3	2
Thyroid	3	2
Eustachian tube	1	0.5
Face	6	3
Breast	6	3
Kidneys	6	3
Peritoneum	1	0.5
Gallbladder	1	0.5
Tonsil	1	0.5

Abdominal manifestations may resemble tuberculous peritonitis, with a serous or, rarely, a chylous ascites. Retroperitoneal involvement may be revealed by the effects of pressure on the vena cava, bowel or nerves. Jaundice may result from pressure on the bile ducts, fluctuating in degree. It is impossible in many cases to distinguish abdominal from retroperitoneal

node involvement; all of our cases, therefore, have been classified as having abdominal node involvement. In most of this group palpable masses were present in the abdomen. In a smaller number, no palpable masses were present but symptoms of abdominal involvement were extremely suggestive in cases where a diagnosis of Hodgkin's disease had already been made from biopsy of a peripheral lymph node. The abdominal and retroperitoneal nodes were involved in 54 per cent of the 185 cases.

The spleen was enlarged in 31 per cent of the 185 cases, and such enlargement was accepted as sufficient evidence of involvement in cases of known Hodgkin's disease. Many authors state that the spleen is involved in 60 to 70 per cent of all cases, usually being diffusely enlarged or containing local foci, which are grossly yellow or gray and suet-like in appearance.

Bone lesions are most often osteolytic and occur in the ribs, sternum, vertebrae, pelvis, humerus, and femur. These lesions are frequently single and appear on the roentgenogram as rarefied cystic areas, sharply demarcated. Occasionally an osteoblastic lesion is present and involves more than one bone. This type responds to treatment less satisfactorily than the osteolytic type. In our series bone lesions, demonstrable by x-ray examination, were present in 20 per cent of the cases. In a series of 257 cases reported by Vieta *et al.* (29), bone lesions were present in 15 per cent; 58 per cent of the lesions were of the mixed variety; 28 per cent were entirely osteoclastic; 14 per cent were purely osteoblastic. The bone lesions may develop by enlargement of foci in bone marrow or by extension of adjacent foci infiltrating or pressing on bony structure. All bone lesions in our cases were demonstrable by x-ray examination or at autopsy.

Nerves and spinal cord can be similarly involved by the spreading lesions, producing pictures difficult to differentiate from neoplastic or other disease. Herpes zoster is a fairly common complication of Hodgkin's disease (6 cases in our series). Lesions in the nervous system were present in 4, or 2 per cent, of our series.

Pregnancies occurred in 4 cases at some time following treatment. In all, 6 children were born to 4 patients.

Tuberculosis in an active or inactive state was present in 6 cases. Tuberculosis and Hodgkin's disease are not infrequently coincidental, as stated by Sternberg (7).

An unusual site of involvement is the breast, according to Adair and Craver (30). These authors found only 8 cases in the literature and added 5 cases, producing a total of 13. There were 6 examples of breast involvement in our series. In one of the cases a breast lesion developed during the course of the disease, and the breast was amputated. Histologic examination revealed the typical structure of Hodgkin's disease. One male patient, aged 27, had a diffuse infiltration of the entire breast, which responded well to therapy. Two patients had nodules in the breast. Another had a large mass in the breast, and the sixth had a diffuse enlargement of the whole breast. While a positive biopsy of the breast lesion was obtained in only one case, the presence of definite masses or infiltration of the breast and their response to x-ray therapy in cases of known Hodgkin's disease are strong evidence in favor of involvement.

TREATMENT

Irradiation either by x-rays or radium is by far the most effective method in the treatment of Hodgkin's disease. The prognosis for cure is uncertain, however, and the term "survival rate" seems the proper one to use in respect to this disease.

Hodgkin's disease is so varied in its manifestations that it is necessary to treat each case individually. Different parts of the body should be treated in different ways, depending upon the accessibility of the involved nodes. Some modification of the treatment is also required in advanced stages. A few basic principles are followed, however, in all cases.

Usually more than one node in a chain is involved, and the whole group should be

treated as a unit. For example, if cervical nodes are involved on one side, it would seem advisable to include the supraclavicular and submaxillary nodes in a single field. Treatment should also be directed to the mediastinum as a whole, rather than being limited to the area where there is a visible mass.

Enlarged nodes usually begin to respond within a few days after the first treatment and may disappear after a relatively small dose. It is likely, however, that some of the abnormal cellular structure indicating activity still remains in the nodes, and a local recurrence will soon be noticed. Since recurrences seem more radioresistant, it is advisable to give a heavier dosage during the initial series to prevent their development. The series should be given in a relatively short time to produce the maximum effect; fourteen days has been arbitrarily chosen as the upper limit. If the treatment can be given in a shorter time without too much ill effect, the results may be even further improved.

A dose of more than 1,000 tissue roentgens is given in almost all cases, in some cases as much as 2,000 tissue roentgens. More than this amount is rarely used.

In the case of cervical nodes, 900 r, in air, is given to each of three fields, an anterior, posterior, and lateral. In the case of the mediastinum, 1,200 to 1,500 r, in air, to each anterior and posterior field is, in our opinion, within the proper range of dosage.

Very large masses of long standing are usually more resistant to radiation than smaller, more recently enlarged nodes and should be treated more heavily. The recently enlarged nodes should, however, be given a certain minimum dosage even though they may respond and return to normal size before the intended amount is administered.

It is impossible to predict future sites of involvement. Isolated areas may become involved, as the scalp or extremities, while the larger chains of nodes are not affected. For this reason, we believe that prophylactic irradiation is contraindicated.

The most favorable cases are those in which only one chain of nodes is involved and thorough irradiation is given after a biopsy has been taken. Slaughter and Craver (26) refer to local resection followed by irradiation as a successful method in this type of case. They reported 5 cases treated in this manner with very satisfactory results. The survival period in these cases was five, six, eight, eleven, and eleven years. (Finzi, 31, stated that the longest survivals were in patients with strictly localized disease who were treated with heavy dosage even after regression of the nodes.) These results suggest that Hodgkin's disease may start as a localized process, the arrest of which may delay development of a generalized disease.

It is reasonable to suppose that heavy x-ray dosage would produce as effective a result as surgery in the case of radiosensitive lesions such as the lymphoblastomas. In most cases x-ray therapy should be more effective, since all the nodes in the chain would be included.

O'Brien (32) observed one patient who had been treated by surgical excision of nodes in 1920. Nineteen years later there was a recurrence in the supraclavicular nodes, associated with a mediastinal mass. The mediastinal mass was irradiated and the supraclavicular nodes were removed with good results. Histologic examination revealed Hodgkin's disease.

When several chains of enlarged nodes are present, the chain causing the most symptoms is treated first. Two groups of nodes may be treated simultaneously.

An interesting observation is the marked response, in some cases, of generalized manifestations, particularly pruritus, fever, and weakness, to treatment of the local lesions. The pruritus often clears rapidly, and the patient's general condition is usually much improved as the local areas respond.

For the peripheral lesions in our cases, 200 or 220 kv. and 0.5 mm. Cu plus 1.0 mm. Al filter have been used, the half-value layers being 0.9 and 1.3 mm. Cu, respectively. For the deeper lesions the filter was increased to 1.0 mm. Cu plus 1.0 mm.

Al, the half-value layers being 1.4 and 1.7 mm.

Total Body Irradiation: The principle of small doses of irradiation to the entire body, or spray irradiation, was described by Dessauer (33) in 1907 and by Chaoul and Lange (34) in 1923. The latter workers used it in 12 cases of Hodgkin's disease with varying degrees of success. A similar method was introduced at Memorial Hospital, New York, in 1931 by Heublein (35) and has been called the "Heublein method." Even moderate doses of x-rays to the entire body in man would, of course, produce deleterious effects. In the animal, one erythema dose led to rapid death. Small doses, however, often resulted in considerable reduction in size of the tumor.

Heublein, in collaboration with Craver and Failla of the Memorial Hospital, devised a method of treating patients with prolonged continuous irradiation with hard roentgen rays at low intensity at a distance of 3 meters, and Medinger and Craver (36) report a series of cases treated by this method. Dosage was about 17 r per day, in air, at a rate of 0.86 r per hour, for an average dose of 100 r. No cases of Hodgkin's disease were treated with the Heublein method alone, because it was considered unwise not to give additional local therapy to each group of enlarged nodes. Ninety-four cases were treated with local therapy and total body irradiation, with an average survival period of forty-two months. For all cases, irrespective of the method of treatment, the average was thirty-four months. In the Heublein series, the five-year survival rate was 24 per cent, which was an improvement of 6 per cent over the complete series of Hodgkin's disease treated at that clinic.

As a result of their observations on total irradiation, Medinger and Craver reached the following conclusions:

1. Total body irradiation alone is not sufficient to produce lasting results.
2. The greater the amount of previous roentgen therapy, the poorer the response to total irradiation.
3. Terminal cases of Hodgkin's disease were unaffected by the treatment.
4. The first few treatments were most beneficial.
5. Maximum improvement resulted where local disease was first controlled by local therapy.

Certain reactions to the x-ray body bath may occur, particularly gastro-intestinal disturbances, weakness, apathy, fever, purpura, and unfavorable blood changes. In patients who have recently received large doses of x-ray and have leukopenia, the method should be used with great caution.

Total body irradiation according to the Heublein technic is extremely impractical in most clinics because of the limited number of x-ray machines available. With this procedure, one machine must be devoted daily to the treatment of only two patients for periods of twenty hours or more. Routine use of the method has not been tried at our clinic. Spray irradiation has been given here at a much higher rate per minute, to a total dosage of 30 r at a target-skin distance of 140 cm., two or three doses constituting a series. Two patients showed remarkable improvement following such treatment, and the improvement lasted long enough so that benefit from local therapy was obtained. In most cases, however, where this type of therapy has been given, the patients were in the terminal stages of the disease and were unimproved.

Treatment According to Systems: In all locations where it is possible, 900 r, in air, should be given to each of three areas. This is applicable in the cervical region. Where there is bilateral cervical involvement, however, considerable care must be exercised in directing the x-ray beams in order to prevent too much concentration in the central area of the neck. Extreme discomfort can be produced by excessive reaction in the pharynx or esophagus, resulting in dysphagia, hoarseness, and dryness of the throat. This reaction reaches its maximum in approximately three weeks. Rather severe skin reaction can occur from the cross-firing of carelessly directed beams in these cases.

Pulmonary involvement is often accom-

TABLE V: SURVIVAL RATE IN HODGKIN'S DISEASE AFTER FIRST TREATMENT
(185 Positive Biopsy Cases)

Year	No. of Cases	Years of Survival																Living
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
1926	2	2	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
1927	3	2	2	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0
1928	5	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1929	8	4	3	3	2	1	1	1	1	1	1	1	1	1	1	1	1	1
1930	7	4	2	1	1	0	-	0	0	0	0	0	0	0	0	0	0	0
1931	16	12	7	6	5	-	-	3	3	3	2	2	1	1	1			1
1932	18	13	11	6	6	4	3	3	2	2	1	1	1	1				1
1933	15	8	7	7	7	7	5	3	2	2	2	1	1*					0
1934	14	11	7	5*	1	1	1	1	1	1	1	1						1
1935	14	8	8	6	5	4	2	2	2	2	1							0
1936	5	2	2	2	2	2	1	1	1	1								1
1937	15	9	7	6	6	4	4	4	4									4
1938	12	10	8	6	4	1	1	1										1
1939	13	4	3	1	1	0	0											0
1940	13	7	6	6	6	6												6
1941	10	6	5	5	5													5
1942	15	7	5	4														4
Cases	185	185	185	185	170	160	147	134	122	107	102	88	74	59	41	25	18	25
Survival		111	85	67	53	33	21	19	16	12	8	6	4	3	2	1	1	
Per cent		60	46	36	31	21	14	14	13	11	8							

* Lost contact with one case.

panied by rather severe dyspnea because of bronchial obstruction due to enlarged mediastinal nodes. In these cases, it is considered unwise to administer the usual 250 to 300 r, in air, to the mediastinum in one treatment, since edema of the bronchi may occur after the first or second treatment, and edema, added to the constriction already present, will result in serious consequences. Hence 50 to 75 r, in air, should be given at the first treatment, the amount being increased gradually with following treatments until the patient can tolerate an average dose. The obstructive lesions usually respond rapidly, with marked relief of dyspnea.

Cases which have received previous roentgen therapy to the mediastinum or lungs may conceivably develop pulmonary fibrosis when given more radiation in the same regions. While this complication is not very common, it should be kept in mind when interpreting follow-up roentgenograms of the chest. The fibrosis may be misinterpreted as a recurrence of Hodgkin infiltration, resulting unjustifiably in further therapy to this region.

Treatment to the abdominal and retroperitoneal lymph nodes results in certain complications which, however, are usually not too serious to prevent completion of a full series. Nausea, vomiting, diarrhea, and other gastro-intestinal symptoms are quite common, especially when the treated areas are large. If widely separated masses are present, they are best treated separately. As previously stated, back pain in a known case of Hodgkin's disease is a sufficient indication for therapy even in the absence of palpable masses.

RESULTS OF TREATMENT

Earlier reports show that the duration of life following the onset of Hodgkin's disease was very short, although some patients were known to live from five to ten years without therapy. In general, the survival period in children appeared to be considerably shorter than in adults, the average being under twenty months.

Following the advent of x-ray therapy, there was a distinct increase in the survival period, by as much as one or two years. According to Krumbhaar (11), records at the University of Pennsylvania show a five-year survival rate of 15 per cent and a ten-year survival rate of 6 per cent following the method of Pendergrass. In this series, one patient was living after twenty-two years—the longest period of survival.

TABLE VI: SURVIVAL RATE IN HODGKIN'S DISEASE AFTER FIRST TREATMENT (53 Clinical Cases)

Year	No. of Cases	Years of Survival 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Living
1926	2	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1927	5	3	3	3	3	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2
1928	4	2	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0		0
1929	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			0
1930	7	5	2	1	0	0	0	0	0	0	0	0	0	0	0	0				0
1931	4	2*	1	0	0	0	0	0	0	0	0	0	0	0	0					0
1932	6	5	4	3	3	2	1	1	0	0	0	0	0	0						0
1933	3	1	1	1	1	1	1	0	0	0	0	0	0							0
1934	2	1	1	0	0	0	0	0	0	0	0	0								0
1935	3	1	1	1	0	0	0	0	0	0	0									0
1936	2	2	1	1	1	0	0	0	0	0										0
1937	4	2	2	1	0	0	0	0	0											0
1938	4	1	1	1	1	1	1*	0												0
1939	0	0	0	0	0	0	0													0
1940	0	0	0	0	0	0														0
1941	3	1	1	1	1															1
1942	3	2	1	1																1
Cases	53	53	53	53	50	47	47	47	43	39	37	34	32	29	23	19	12	11	7	4
Survival		29	21	16	11	7	5	3	2	2	2	2	2	2	2	2	2	2	2	2
Per cent		55	40	30	22	15	11	6	5	5	5	5								

* Lost contact with one case.

In Craver's (26) series of 265 cases, the five-year survival rate was 18 per cent and the ten-year rate 3 per cent. The average survival for all the cases was 33.8 months from the beginning of x-ray therapy. This series evidently includes the 94 cases previously mentioned which were treated by the Heublein total irradiation technic, with an average survival of forty-two months from the institution of therapy and a five-year survival rate of 24 per cent. Without the inclusion of these cases so good a survival rate would obviously not have been obtained. They probably represent the most favorable results recorded anywhere in the literature.

In our series of 185 cases proved by biopsy (Table V), the five-year survival rate was 21 per cent and the ten-year survival rate 8 per cent. The average duration of life from the institution of therapy was 33.1 months, which is slightly less than the average of 33.8 for Craver's entire 265 cases. His cases were all followed for a period of longer than five years, while our series includes some living patients who have been followed for only three years. Our five-year survival rate is a 3 per cent improvement over the Craver series (Table VII).

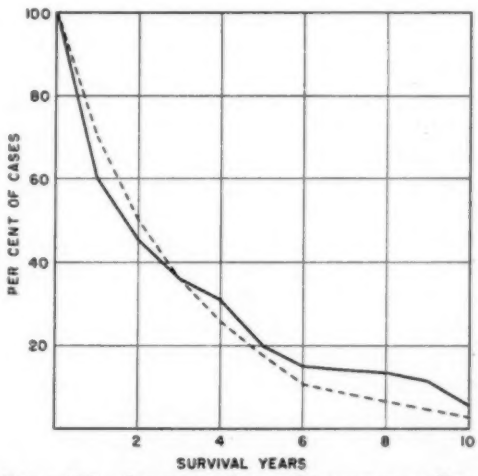

TABLE VII: SURVIVALS AFTER TREATMENT IN TWO SERIES OF HODGKIN'S DISEASE. SOLID LINE REPRESENTS UNIVERSITY OF MINNESOTA HOSPITALS SERIES (185 CASES). BROKEN LINE REPRESENTS MEDINGER AND CRAVER'S SERIES (ALL TREATED CASES).

Ewing (37) gave the average survival of untreated patients as about eighteen months. A series of 52 cases of untreated Hodgkin's disease collected by Craft (39) from the autopsy records at the University of Minnesota Hospitals showed a five-year survival rate of 6 per cent from the time of onset. There were no ten-year survivals in this group.

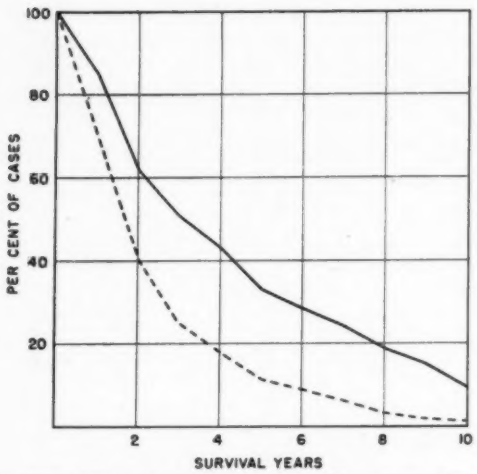

TABLE VIII: SURVIVALS AFTER ONSET IN TWO SERIES OF HODGKIN'S DISEASE. SOLID LINE REPRESENTS UNIVERSITY OF MINNESOTA HOSPITALS SERIES (171 CASES). BROKEN LINE REPRESENTS MINOT'S SERIES OF UNTREATED CASES.

It will be noted in Table VI that for 53 cases in which positive biopsies were not obtained at this clinic, the five-year survival rate was only 15 per cent. This is considerably less than the survival rate in the positive biopsy group, which may be largely due to the inclusion of cases which were not truly Hodgkin's disease.

An estimate of the duration from onset of the disease was made in 171 cases in which the time of onset could be determined. The five-year survival rate in this group is approximately three times as great as in a series of untreated cases of lymphoblastoma of all types reported by Minot (38). The interval between the onset and the first treatment in our 171 cases was 15.5 months (Table VIII).

Of 5 patients surviving more than ten years from the beginning of treatment, 4 are still alive, the longest period of survival being sixteen years. Others are living eleven, thirteen, and fourteen years after the first treatment. The patient surviving sixteen years had enlarged nodes in the cervical and axillary regions which were treated in August 1929. There has been no recurrence since that time. The lesions were apparently localized and were adequately treated.

A patient surviving for fourteen years was given radiation to the axilla, abdomen, mediastinum, and spleen over a period of three years, beginning in 1931 at the age of twelve. No recurrences were noted until 1943, when enlarged nodes in the cervical and axillary regions were treated. A mass again developed in the supraclavicular region in July 1945 and was presumed clinically to be recurrent Hodgkin's disease. After removal, however, microscopic examination revealed the characteristic structure of neurofibroma. The patient was living and well in December 1945.

A total of 387 cases of all types of lymphoblastoma (Table IX) had been treated

TABLE IX: LYMPHOBLASTOMAS AT THE UNIVERSITY OF MINNESOTA HOSPITALS, TO THE END OF 1942

	Dead	Living	Total
Lymphoblastomas (unclassified)	44	16	60
Lymphosarcomas	57	18	75
Aleukemic leukemias	13	1	14
Hodgkin's disease	209	29	238*
TOTAL	323	64	387

* Hodgkin's disease 62 per cent of total.

at this clinic up to the end of 1942. Of the total number, 238 or 61.5 per cent were Hodgkin's disease. The percentage of patients with Hodgkin's disease still living is considerably less than for the other lymphoblastomas with the exception of the aleukemic leukemias, the number of which is too small for an accurate estimate of the response.

CASE REPORTS

CASE I: S. T., female, aged 28, was admitted to the hospital in September 1932 with a history of enlargement of the cervical nodes bilaterally over the previous eighteen months. Dyspnea of mild degree had been present about two months. Biopsy of the cervical nodes revealed the characteristic structure of Hodgkin's disease, including Dorothy Reed cells. An x-ray film of the chest demonstrated a mass in the upper mediastinum. The cervical nodes and mediastinum were treated, with good response.

In February 1937, a mass developed in the soft tissues over the sternum on the right. The mass was firm and painless and measured $5 \times 6 \times 3$ cm. It responded well to treatment, completely subsiding within two months.

In October 1939, a mass appeared below the left clavicle and an additional small mass in the right hilum. Both lesions were treated with satisfactory results.

In May 1941, inguinal nodes on the right were treated. In August 1941, pain of rather severe degree occurred in the lumbosacral region. X-ray examination revealed partial destruction of the body of the 4th lumbar vertebra. This area was treated with the usual dosage, producing partial relief of pain. In the meantime, a large hard mass developed in the left mid-abdomen, probably representing enlarged retroperitoneal nodes. After therapy to this region, the mass entirely disappeared. The patient's health was quite good from November 1941 until August 1942, when mild pain occurred in the left flank. The pain continued until a visit to the clinic in March 1943. A film of the lumbar spine showed partial destruction of the body of the first lumbar vertebra and 12th rib on the left. Treatment to this area gave considerable relief of pain.

Re-examination of the chest in May 1944 revealed an infiltrative lesion in the right base. Intensive therapy was given to this region with good results.

In March 1945, on readmission, severe back pain in the upper lumbar region with radiation of pain anteriorly was described. X-ray examination revealed further destruction of the 12th rib on the left and the 1st lumbar vertebra, and an osteoblastic lesion in the body of the 1st lumbar vertebra, not previously present. On the sixth day after therapy, the patient said she had complete relief of pain. She has remained well since that time. It is now over thirteen years since the first treatment was given and multiple areas have been treated.

CASE II: V. N., a 59-year-old man, was admitted to the clinic in 1926, with a mass of enlarged nodes in the right cervical region. A biopsy specimen was diagnosed by Dr. Bell as a cellular type of Hodgkin's disease. The patient responded well to x-ray therapy but had a single recurrence in the same region several months later which responded less rapidly. Death from pulmonary tuberculosis occurred in 1942. Because of the possibility that the original lesion was tuberculous in origin, this case was not included in the series of 185 proved cases.

SUMMARY AND CONCLUSIONS

A series of 185 cases of Hodgkin's disease proved by biopsy has been reviewed in detail. Statistical evidence has been presented to indicate the multiple areas involved by Hodgkin's disease throughout the body. The peripheral lymph nodes are most frequently affected, followed by mediastinal nodes, abdominal nodes, spleen, and bones. The disease is most common in the third decade, and about two-thirds of the patients are males.

A method of irradiation therapy has been developed at this clinic, which we believe is very efficient in the treatment of the lymphoblastomas. Treatment is considerably more intensive than in most series reported. A full course of therapy is applied to each area of involvement, the dosage varying between 1,000 and 2,000 tissue roentgens over a period of fourteen days. Large masses are treated more intensively, and the group of enlarged nodes causing the greatest distress is treated first. Prophylactic irradiation, in our opinion, is contraindicated.

The five-year survival rate from the time of treatment in our cases was 21 per cent and the ten-year rate 8 per cent, a high figure as compared with other series. Other statistics have also been presented, demonstrating the marked increase in the survival period from the onset of symptoms in treated cases as compared with a series of untreated cases of lymphoblastoma reported by Minot in 1926.

The unpredictable nature of Hodgkin's disease is recognized and claims of cure cannot be made. Roentgen therapy has, however, markedly increased the survival rate.

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The Early Effects of X-Rays on the Ovaries of the Rat[1]

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IRRADIATION of the ovaries with a sufficient dose of x-rays leads, after a certain time, to degenerative changes in these organs (1, 5, 6). Halberstaedter (2), in 1905, found in rabbit ovaries, ten to fifteen days after irradiation, disappearance of graafian follicles and degeneration of primary follicles, the numerous interstitial cells of the rabbit ovary being relatively resistant to x-ray irradiation.

As regards alterations in the ovary in the first few hours following irradiation, a diversity of opinions exists. Reifferscheid (7) described alterations in the ovary of the mouse as early as three hours after irradiation. According to him, numerous pyknoses are visible at this time in the cells of the granular layer in the large follicles, which later degenerate and undergo lysis within the follicular cavity; at the same time, the nucleus of the ovule loses its normal configuration. Müller (4), however, has argued that the alterations observed by Reifferscheid cannot be ascribed to the action of x-rays, since similar observations have been made in ovaries of non-irradiated mice and guinea-pigs. On the other hand, certain authors have confirmed the findings of Reifferscheid twenty-four hours after irradiation (3). On the whole, the evidence concerning the early effects of irradiation on the ovary has been based on quantitative rather than qualitative changes. In fact, Reifferscheid (9) himself has recognized that the alterations described following irradiation may also be observed in normal ovaries, but in far less degree.

In view of the existing diversity of opinion concerning early lesions of the irradiated ovary, we have carried out histologic examinations of ovaries of normal and irradiated rats with a view to ascertaining whether there is any difference in the distribution of the pyknoses in the follicles.

METHOD AND TECHNIC

The histologic studies were performed on ovaries of the following groups of highly inbred albino rats.

A. Control group: 4 rats.

B. Experimental groups: Rats irradiated with 50 to 2,000 r.

(*a*) Seven rats, irradiated in the region of the abdomen, the ovaries being exposed directly to the action of the x-rays.

(*b*) Two rats, irradiated in the region of the cephalothorax, the ovaries being protected from direct exposure by means of a lead plate.

(*c*) Two young rats, irradiated totally.

The radiation was delivered from a Machlett therapy x-ray tube, operated on a multivolt apparatus at 150 kv., 4 ma., Al 0.5 mm., distance 30 cm., 100 r/min.

The animals were killed four hours after irradiation. Ovaries were fixed in Bouin's fluid and sectioned after embedding in paraffin. The sections were mounted on slides in complete series and stained with iron hematoxylin (according to the method of Masson) and eosin.

Microscopic preparations were examined in series so as to obtain a complete picture of each follicle, including the ovule and its nucleus.

DESCRIPTION OF MICROSCOPIC PREPARATIONS

In the examination of the microscopic preparations our attention was especially directed to follicular cells of primary follicles and the granular layer of large follicles. At the same time an attempt was made to elucidate the relationship between

[1] From the Department of Radiobiology (Cancer Laboratories), Hebrew University, Jerusalem. Aided by a grant of the British Empire Cancer Campaign. Accepted for publication in June 1946.

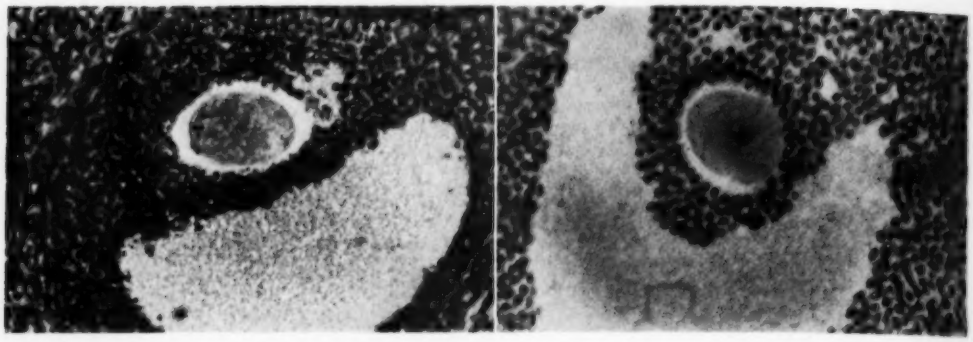

Fig. 1. Control rat. Graafian follicle with numerous pyknoses in the granular layer. The nucleus of the ovum is in mitosis. ×225.

Fig. 2. Control rat. Graafian follicle with the ovule in a resting state. There is almost total lack of pyknosis in the granular layer. ×225.

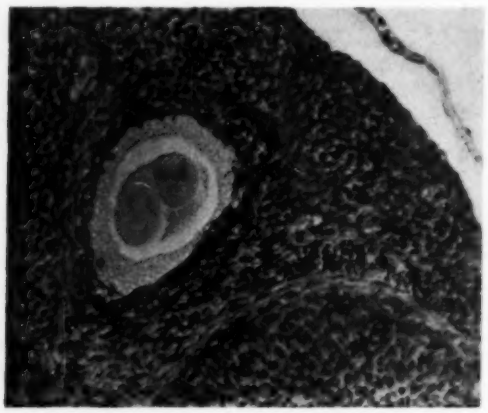

Fig. 3. Control rat. Atresic follicle with degenerate cells representing the residue of the ovule. ×190.

the state of the nucleus of the ovule and the condition of the follicular cells.

A. *Control Rats:* Our description of normal ovaries represents the total findings in four controls: (*a*) one rat weighing about 150 gm., (*b*) two rats weighing about 100 gm., and (*c*) one small rat weighing 60 gm. Only the more striking features and those which furnish a suitable basis for the evaluation of the effect of radiation will receive emphasis in the following description.

The ovaries contained numerous follicles in varying degrees of development. One finds in a normal ovary follicles of different size, *viz.*, primary follicles, stratified follicles, as well as graafian follicles. In addition, there are atresic follicles well on the way to disappearance. The *primary follicles* generally contain an ovule whose nucleus is in the germinative vesicle state, with a nucleolus. The layer of follicular cells frequently shows mitotic figures and rarely a pyknotic nucleus. *Stratified follicles* similarly contain an ovule with a resting nucleus and have a granular layer which exhibits numerous mitoses and some pyknotic cells. Among the large graafian follicles, two types can be distinguished on the basis of the presence of pyknosis in the granular layer. In one pyknoses are numerous, whereas in the other only a few are visible. This difference is brought out especially clearly when the entire series of sections of an ovary is examined. In one ovary we found a marked pyknosis of the granular layer in nearly one-half of the graafian follicles and a very slight one in the remaining half. When the total number of graafian follicles in an ovary is examined in series, it becomes apparent that the pyknotic follicles contain dividing ovules and nuclei in different stages of mitosis (Fig. 1). On the other hand, graafian follicles with slight pyknosis contain resting nuclei (Fig. 2). The more advanced state of division of the ovule, the greater is the number of the pyknotic follicular cells.

In the *atresic follicles*, the granular layer is almost completely gone, but residues of

the pyknotic debris can be seen. In the contracted cavity of the atresic follicles two or more large degenerate cells representing the residue of an ovule which probably underwent an abnormal series of divisions may be seen (Fig. 3).

B. Irradiated Rats, Group a: Adult rats weighing 150 gm. were irradiated in the region of the abdomen. One animal received 50 r, another 200 r, another 400 r, and four 2,000 r each. The histologic findings four hours after irradiation in the rats which received 50 and 200 r were identical with the findings in the non-irradiated controls. The following description summarizes the observations on the ovaries of the animals irradiated with 400 r and 2,000 r, respectively.

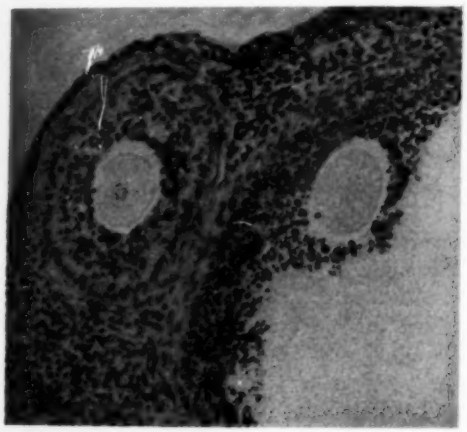

Fig. 4. Rat irradiated with 2,000 r. Young follicle and a graafian follicle exhibiting pyknoses of the follicular cells. ×190.

Rat 3, of medium weight (150 gm.), was irradiated in the region of the abdomen with 400 r. The cephalothoracic region was protected from direct exposure by means of a lead plate. The animal was sacrificed four hours after the irradiation. The histologic examination revealed a cellular lesion which was manifested as a pyknotic reaction in the follicular cells of the follicles. Pyknoses were evident in primary follicles which did not show alterations of the ovule. In the most developed follicles, *i.e.*, the stratified follicles, a number of pyknoses were also exhibited. The ovules of these follicles had a practically normal appearance. The graafian follicles in most cases presented numerous pyknoses. These were especially numerous and were found constantly in follicles which contained a mitotic ovule. When the ovule was in a resting state, on the other hand, the pyknoses were not always equally numerous. Only a certain number of these follicles showed numerous pyknoses. Follicles could also be observed in a state of degeneration, with large cells representing the residue of an abnormally divided ovule.

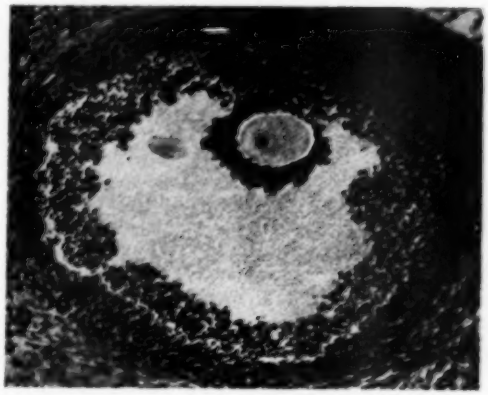

Fig. 5. Rat irradiated with 2,000 r. Graafian follicle with numerous pyknoses in the granular layer. The nucleus of the ovum is in a resting state. ×125.

Rat 18, of medium weight (150 gm), received 2,000 r in the region of the abdomen, the cephalothoracic region being protected by means of a lead plate. The animal was killed four hours after irradiation. The ovary contained numerous follicles in different stages of development. The pyknotic lesions in the follicles were very pronounced. Some young follicles and those in an advanced stage of development exhibited numerous pyknoses in the granular layer (Fig. 4). Pyknoses were found in all follicles, irrespective of the state of development of the contained ovule. Follicles with a dividing ovule and with a resting ovule (Fig. 5) were affected to an almost equal degree. Some of the follicles undergoing atresia exhibited the usual picture of an abnormal dividing

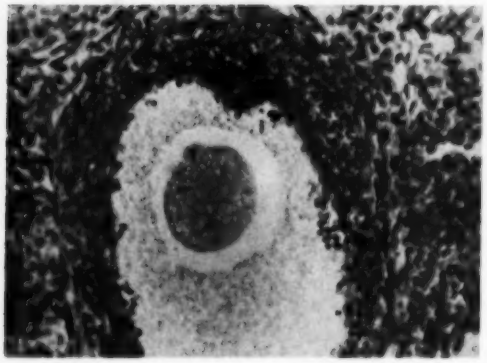

Fig. 6. Rat irradiated with 300 r. Atresic follicle with an ovule containing a dividing nucleus with a globular polar body. ×225.

ovule. In the corpora lutea no demonstrable lesion was found.

Rats 26, 27, and 28, which received the same dosage of x-rays and were killed after four hours, showed the same microscopic picture as rat 18.

Irradiated Rats, Group b: This group consisted of 2 rats, irradiated in the region of the cephalothorax.

Rat 10, of medium weight (150 gm.), received 400 r in the region of the cephalothorax. The abdominal region, in which the ovaries lie, was protected from direct exposure by means of a lead plate. The animal was killed after four hours. On microscopic examination, the ovary was seen to contain follicles in different stages of development. There were numerous corpora lutea. The young follicles showed no alterations which could be ascribed to the effect of x-rays. The developed follicles presented two aspects: (*a*) follicles with pyknotic cells and ovules in a state of division and (*b*) cells of the granular layer with few pyknoses and containing a resting ovule. In general, the picture is one which can be observed in a non-irradiated ovary.

The ovary of a second rat irradiated in the same manner showed the same microscopic picture.

Irradiated Rats, Group c: Two young rats were irradiated totally with 50 and 300 r, respectively. The animals were sacrificed four hours after irradiation.

Rat 4, weighing only 60 gm., received a total dose of 50 r. Histologic examination revealed no lesion which could be attributed to the action of x-rays. The young follicles showed no alteration, while in the graafian follicles the alterations were of a type observed in graafian follicles of non-irradiated ovaries, namely a few pyknoses in follicles containing a resting ovule and numerous pyknoses in the granular layer of follicles with a dividing nucleus.

Rat 5, also weighing about 60 gm., received a total x-ray dose of 300 r. The histologic examination disclosed pyknotic lesions in most of the follicles. One or two of the large follicles were free from pyknotic lesions. In the majority of cases the granular layer of the follicles exhibited a marked pyknotic reaction independently of whether the contained ovule was in a state of division or rest. A large number of atresic follicles, some with ovules containing a dividing nucleus with globular polar bodies (Fig. 6) and some with large cells in a state of degeneration, were evident.

DISCUSSION

Our histologic examinations show that follicles with signs of degeneration are normally present in the ovary of the rat. The degenerative process begins with appearance of numerous pyknoses in the cells of the granular layer of the follicle, which undergoes lysis within the follicular cavity. Following the pyknotic destruction, the granular layer becomes thinner and finally disappears, leaving debris of pyknotic nuclei. The appearance of numerous pyknoses coincides in time with the presence of mitotic figures in the ovule. The degree of the pyknotic degeneration of the granular layer is the greater the more advanced is the state of division of the ovule.

These degenerative changes in the ovary resemble those observed by Reifferscheid a few hours after irradiation. It is entirely comprehensible, therefore, that Müller should have doubted their relation to irradiation. However, it seems to have escaped both authors that in non-irradiated ovaries pyknoses are largely restricted to

follicles whose ovules are in a state of division. When the follicles are examined in entirety, it becomes evident that pyknoses are normally very rare in the granular layer of follicles whose ovule contains a nucleus in a resting state (Fig. 2) and that they are numerous in follicles whose ovule contains a nucleus in a state of division (Fig. 1). The evaluation of the effect of x-rays on the ovary is best made, therefore, on the basis of findings in follicles which contain an ovule with a resting nucleus.

Our observations have shown that four hours following irradiation numerous pyknoses are evident in the granular layer of the large follicles irrespective of whether the nucleus of the ovule is in a state of division or rest (Fig. 5). Pyknoses were found, moreover, in follicular cells of young follicles in rats which had been irradiated (Fig. 4), but never in corresponding follicles of non-irradiated rats. The impression was further obtained that follicles whose ovule is in a state of division show pyknoses in cells of the granular layer more frequently after irradiation than normally. This impression by itself would lack conviction were it not accompanied by the further observation that pyknoses occur following irradiation in follicles whose ovules are in a state of rest. The general conclusion may be drawn that a sufficient dose of x-rays produces lesion of the ovaries of a rat as early as four hours after irradiation.

The results were best defined with doses of 2,000 r delivered in the abdominal region. A pronounced pyknotic lesion was also observed in the rat which received 400 r (rat 3) in the abdominal region. On the other hand, the rats given 400 r in the cephalothoracic region did not exhibit similar pyknotic lesions. It is our impression, therefore, that the reaction of the ovary is not the same when it is not directly exposed to the x-rays.

No demonstrable difference was found between ovaries irradiated with doses of 50 and 100 r and non-irradiated ovaries. Doses of this magnitude are probably too low to evoke pyknotic lesions in the ovary within an interval of four hours.

SUMMARY

In ovaries of normal rats, pyknosis in the granular layer is generally restricted to follicles whose ovule contains a nucleus in a state of division. Four hours after irradiation with a sufficient dose of x-rays, pyknoses are also in evidence in follicles whose ovule contains a resting nucleus, as well as in primary follicles.

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A Roentgenkymographic Study of the Heart in Myasthenia Gravis[1]

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THE ROENTGENKYMOGRAPH has been established as a helpful adjunct in the study of certain diseases of the heart. It is generally recognized that the main value of this instrument is its ability to record permanently the motion of an organ observed fluoroscopically.

In 1939, changes in the cardiac motion of a patient with myasthenia gravis were detected by the author fluoroscopically while examining the effects of prostigmine on the hypopharynx (4). Inasmuch as all previous cardiac studies in myasthenia gravis had been reported negative (8), the observation was considered preliminary until the kymograph, by recording the pulsations objectively, appeared to confirm the finding. Similar observations were then made on several other patients with myasthenia gravis. The kymograms showed a slight slowing of the pulse, with minor but definite changes in the waves along the left ventricular border after a test dose of prostigmine. In normal young adults used as controls, kymographic changes similar to those found in myasthenia gravis patients could be obtained by the same technic. This indicated that we were dealing with a pharmacologic action of prostigmine and not a sign characteristic of a specific disease entity.

Further studies then were carried out. An effort was made to detect minor differences in the kymographic wave forms of normal subjects as compared with myasthenia gravis patients, and an explanation was sought for the kymographic changes observed following a test dose of prostigmine[2] when other cardiac studies were negative in the same patients.

The work was stimulated by a personal communication from Dr. Sidney Lange of Cincinnati, who had previously made a single cardiac roentgenkymogram on one of his patients with myasthenia gravis. Although the kymogram showed changes which he was unable to explain, he did not consider the single observation of sufficient importance to justify publication. To our knowledge, Dr. Lange is the only previous worker to use the roentgenkymograph in the study of this disease.

The purpose of this paper is to record our findings and to call attention to certain variables which limit the use of the kymograph in studies of this type.

METHOD

Four normal persons and 16 patients with myasthenia gravis were examined. The patients with myasthenia gravis had been extensively studied at the Myasthenia Gravis Clinic of the Massachusetts General Hospital and represented typical cases of the disease.

If the patient had been receiving prostigmine, this drug was withdrawn for twelve or more hours before the examination. During this period symptoms of lassitude, general muscle weakness, ptosis, dysphagia, dysarthria, and other signs of myasthenia gravis usually developed. A roentgenkymogram of the heart was then made. If the initial film was satisfactory, 1.5 to 2.0 mg. of prostigmine methylsulfate with 0.6 mg. of atropine sulfate was given intramuscularly (5). Fifteen minutes later a second roentgenkymogram was obtained.

A roentgenkymograph of the fixed grid type was employed. The average exposure time was one and a half seconds, but this figure was reduced for patients with tachy-

[1] From the Myasthenia Gravis Clinic, Massachusetts General Hospital. Read by title at the Thirty-first Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 9–10, 1945.

[2] The prostigmine was furnished by Hoffman-LaRoche, Inc.

cardia and increased for patients with bradycardia. The exposure time in any individual case, however, was not varied. A rotating-target x-ray tube, operating at 150 ma. and 55–70 kv., was so placed as to provide a 28-inch target-film distance. Par-speed intensifying screens were used. An immobilizing band was found particularly useful in patients with pronounced muscle weakness. Exposures were made with the patient standing in the upright position facing the film and holding his breath in full inspiration. Care was taken to duplicate the radiographic technic as accurately as possible before and after the prostigmine was given.

In order to obtain strictly comparable films, to evaluate artefacts due to cardiac rotation, several exposures were necessary in some patients, especially those having severe symptoms. Only one patient was excluded from the series. In this case, the kymograms made with the patient horizontal, because of extreme weakness, were useless for comparison on account of artefacts in the kymographic waves due to a high diaphragm and cardiac rotation. As the study progressed, it was noted that relatively minor changes in exposure technic, positioning of the patient, and the height of the diaphragm tend to impose greater difficulties in chest kymography than in routine chest roentgenography. Short tube-film distances distort and magnify not only the individual kymographic waves but also the aberrations in the waves due to the above factors. Although teleroentgenkymography has been successfully used by Ungerleider and Gubner (9) to eradicate the difficulties imposed by a short tube-film distance, most x-ray departments do not possess a tube capable of tolerating the high energy necessary for such a procedure.

In order to identify possible sources of error due to the above factors, each pair of kymograms in this study was analyzed according to a predetermined routine. The details on each film were recorded on a large chart in ruled columns which included the following headings: (1) case number; (2) rotation of patient; (3) height of diaphragm; (4) transverse cardiac diameter in systole and diastole; (5) wave amplitude in millimeters on corresponding points along the aortic, right auricular, and ventricular borders; (6) wave forms in the same areas. Having recorded these observations for each case, the data were reorganized in charts to determine the frequency of occurrence of the various findings, the variations between the individual cases, and the coincidence of common findings in the various columns. Although the number of cases examined was small, the data were considered sufficient to demonstrate or to rule out the presence of any characteristic kymographic sign of myasthenia gravis.

RESULTS

Cardiac and Thoracic Measurements: In a previous study (8) it was found that orthodiagrams of the heart show no significant changes in patients with myasthenia gravis.

In this study the transverse diameters of the heart in both the systolic and diastolic phases were made routinely. When the cases showing any degree of rotation or change in diaphragm were excluded, no constant changes in the diameter of the heart or in wave amplitude in any portion of the heart were observed following the administration of the prostigmine test dose.

An attempt was made to estimate and compare the areas of the heart in systole and diastole by tracing the cardiac contours through the peaks and troughs of the waves as suggested by Stumpf (6) and others (2, 3). This method was found unreliable because of the difficulty in outlining the caudal and cephalic borders of the heart. Other workers (1, 7) have encountered the same difficulty especially when the kymograms are made with a short tube-film distance.

The patients with myasthenia gravis frequently showed a slightly increased chest diameter or a slightly lower diaphragm at deep inspiration after a prostigmine injection. This observation was con-

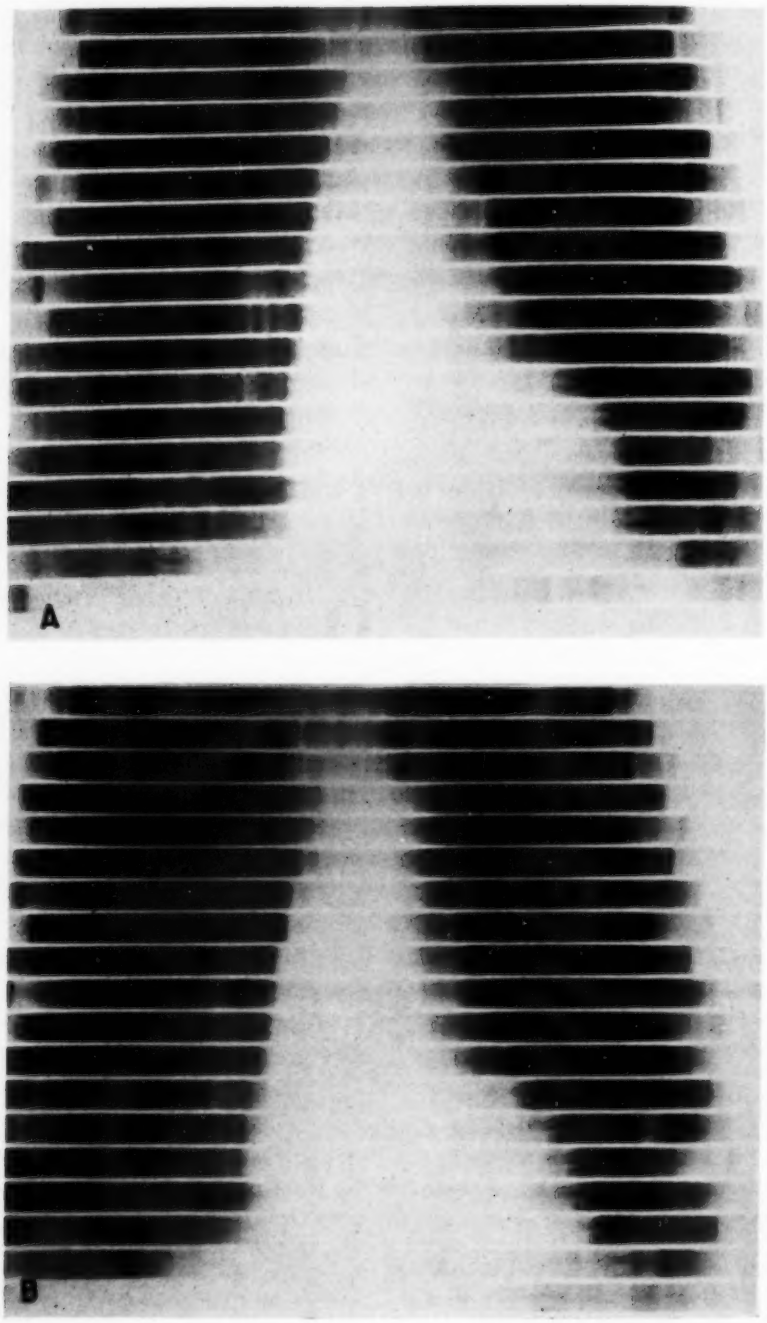

Fig. 1. A. Cardiac roentgenkymogram of patient with myasthenia gravis. Note spike-like configuration of waves along left ventricular border.

B. Same patient after prostigmine test dose. The heart rate has become slower. The spiking of the left ventricular waves has disappeared. The diastolic limbs are smoother and have changed from concave to convex.

firmed teleroentgenographically and is consistent with the general picture of myasthenia gravis.

Heart Rate: Quantitative determinations of the heart rate are not usually made with the roentgenkymograph because of the practical and technical limitations of the method. Stethoscopic or sphygmometric methods are obviously to be preferred. Two or more kymograms made with identical grid speeds, however, are sensitive qualitative indicators of a slight change in heart rate. A slowing of the rate is indicated by a reduction in the number of waves per frame or by the amputation of part of a kymographic wave (Fig. 1), whereas an accelerated heart rate is indicated by a relative increase in the number of waves per frame.

Of the 15 patients with myasthenia gravis, 10 showed a slight decrease in heart rate after the injection of prostigmine. The normal subjects showed a similar decrease after the same medication. It is significant, as will be discussed later, that the 4 cases showing no change in rate also showed no changes, or relatively minimal changes, in wave form.

The slight retardation of the heart rate by prostigmine is one of the pharmacologic actions of this drug. The prostigmine test dose as used in this study has been thoroughly investigated. A small amount of atropine was included routinely to counteract the disagreeable side effects of prostigmine, such as abdominal cramps, diarrhea, diaphoresis, etc. Large amounts of atropine usually quicken the rate. It is felt that the amount of atropine used in our test doses was not sufficient to neutralize completely the bradycardiac action of prostiginine.

Wave Form Changes: The normal kymographic wave forms in various portions of the cardiac contour have been described many times. The pathologic changes in these waves due to aortic insufficiency, pericardial adhesions, cardiac infarction, and other conditions are also well established. The minor changes, however, within the normal variations of the kymographic wave form have been the subject of much speculation and misunderstanding. Many writers have attempted to associate these changes with abnormal physiologic processes. It is the author's opinion that such minor changes must be subjected to unusually careful scrutiny and care in interpretation. The changes observed in myasthenia gravis fall into this category.

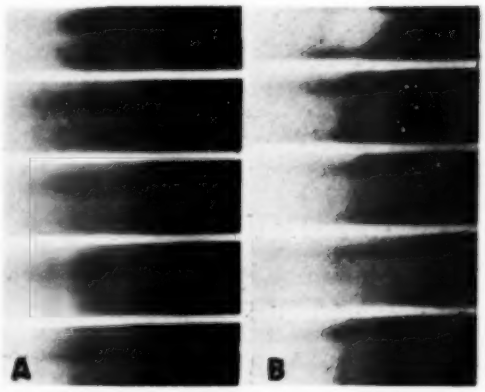

Fig. 2. Left ventricular wave changes in another patient (A) before prostigmine and (B) after prostigmine. These changes resemble those seen in Figure 1. Similar but less marked changes were observed in five other patients and also in the normal individuals studied

The cases in this series showed no remarkable changes in the waves of the aortic and auricular areas except for slight slowing of the rate. Very definite changes, however, were observed in the ventricular waves. Figure 1A is the roentgenkymogram of a patient with myasthenia gravis, while Figure 1B shows the same patient after the administration of a prostigmine test dose. In Figure 2 the left ventricular waves of another patient with myasthenia gravis have been enlarged and illustrate the changes more clearly. One notices, first, that the prostigmine slowed the cardiac rate; second, the peaks lost their spike-like configuration; third, the diastolic limbs became smoother and more convex. Changes of this type were observed in 7 of the 15 cases studied.

That these changes are not constant is shown by Figure 3, which illustrates some of the variations in the left ventricular wave which were encountered. In Case 60

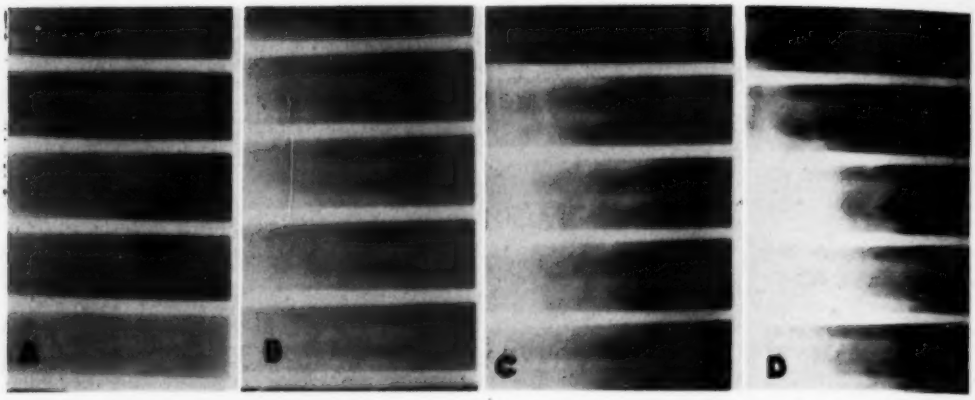

Fig. 3. Other types of left ventricular wave changes observed. For description, see text.

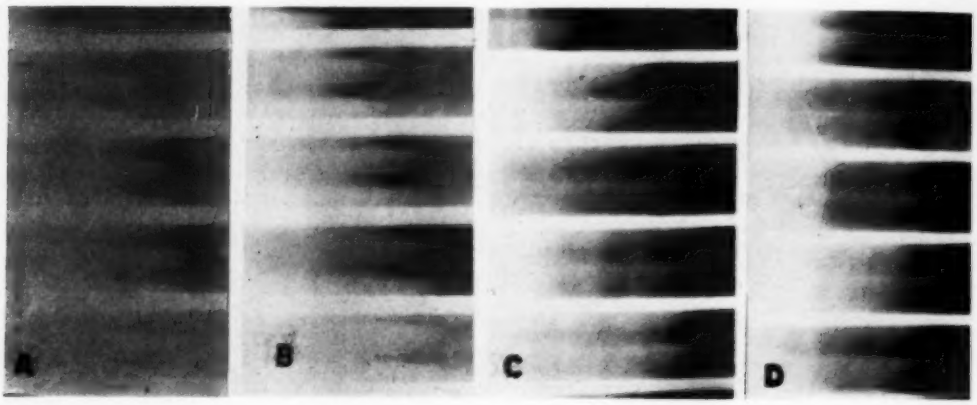

Fig. 4. Left ventricular waves in a patient showing no change in heart rate and no significant changes in wave form after prostigmine test dose.

(Fig. 3 A and B), the prostigmine slowed the rate, the deep biconvex waves along the left ventricular border became shallower, the systolic limbs became flatter and slightly concave, and the diastolic limbs in the lower frames showed a small convex notch. In Case 51 (Fig. 3 C and D), the heart rate was slowed, and the concave contour of the diastolic limb became concavo-convex. Other cases not illustrated here showed varying combinations of the minor wave changes described above.

DISCUSSION

Experienced kymographers will recognize that Figures 1, 2, and 3 show wave forms which are frequently encountered in normal subjects. Pleikart Stumpf (6) has sketched various types of normal waves in his original contribution on kymography. In comparing his illustrations with the wide variety of wave forms found in these cases of myasthenia gravis, it must be concluded that there is no cardiac roentgenkymographic wave form characteristic of this disease.

The reason for the change in wave form after prostigmine, however, remains to be explained. The literature contains no reports concerning the effects of prostigmine on the cardiac roentgenkymogram. The simplest explanation for the type of change in wave form in Figures 1 and 2 was suggested by the fact that the four patients

who showed no change in heart rate after prostigmine also showed no significant changes in wave form (Fig. 4). It is well known that any change in the ratio between the grid speed and the heart rate will affect the appearance of a kymographic wave. If the wave changes in our cases could be explained simply by a change in the grid speed-heart rate ratio, then it would follow that no change in wave form should occur in these individual hearts if the grid speed were so adjusted as to maintain a constant ratio with the heart rate before and after administration of prostigmine.

To test the validity of this assumption, 2 myasthenia gravis patients and one normal person were studied before and after prostigmine with various grid speeds. The results in all 3 cases were remarkably identical. In Figure 5 A and B, the left ventricular waves seen in Figure 1 A and B, respectively, are reproduced. The kymogram 5 C was made a few seconds after 5 B, under identical conditions except that the grid speed was reduced in rough proportion to the degree of slowing of the heart which had occurred. The wave forms in 5 C are almost identical with those in 5 A. This indicates, therefore, that the major changes in the shape of the kymographic wave produced by prostigmine represent artefacts due to the changing ratio between the grid speed and the heart rate.

Precise comparative analyses of the wave forms in 5 A and 5 C, however, still reveal some minute differences. These minute differences varied widely from case to case. It would be illogical to attribute such a wide variety of wave form changes to the action of prostigmine or to any particular physiologic theory. It is more reasonable to attribute such a variety of minor changes in wave form to the uncontrollable variables and limitations of the technic itself.

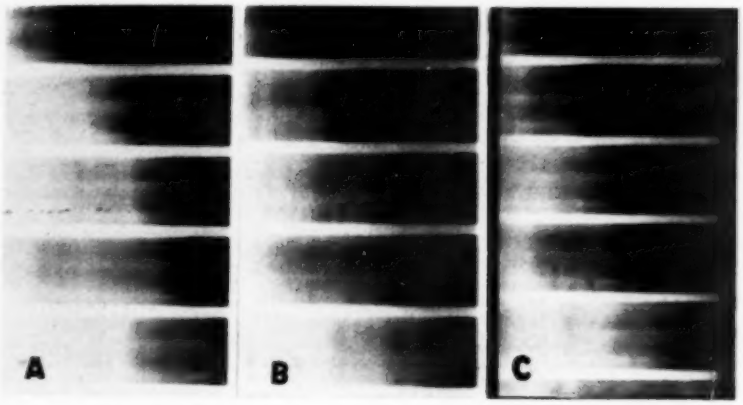

Fig. 5. The reason for the apparent changes in wave form in Figures 1 and 2 is explained here: A and B are enlargements of the left ventricular waves in the case illustrated in Figure 1. C was made a few seconds after B but the grid speed was decreased in proportion to the degree of cardiac slowing. Note that the waves in C have practically reassumed their original configuration.

Limitations of the roentgenkymographic method are particularly noticeable when the auricular and aortic areas are examined. The waves in these areas are extremely variable, deceptive, and frequently difficult to interpret. In the average kymogram these particular waves often do not exceed 1.0 mm. in amplitude, rarely more than 3.0 mm. The superimposed vertebrae and mediastinal structures frequently obscure wave detail. Motion in any portion of the cardiac border is the result of several directional forces and does not represent the true intrinsic pulsation of one chamber. Auricular waves frequently ap-

pear blurred and are often complicated by the distorting effect of transmitted ventricular pulsations. Aortic waves, although more distinct than auricular waves, are determined and influenced by such components as thrusts of blood from the left ventricle, contraction of the aortic wall, aortic tortuosity, and the effects of other stationary and moving mediastinal structures. We have observed pronounced changes, furthermore, in the aortic and auricular waves of normal persons due to relatively minor variations in the tube centering, placement of the subjects, and respiratory phase. These comments, however, are not meant to discourage the use of the kymograph. Rather is it our purpose here to reiterate the limitations and sources of error when an attempt is made to explain minor irregularities in the shape and contours of the individual kymographic waves.

CONCLUSIONS

1. There are no characteristic findings in the cardiac roentgenkymograms of patients with myasthenia gravis.

2. The prostigmine test dose produces no characteristic cardiac kymographic wave changes either in myasthenia gravis patients or in normal subjects. The test dose may slow the cardiac rate somewhat, thereby producing deceptive changes in wave contour.

3. Care and conservatism are urged in the interpretation of changes in the shape and contour of individual kymographic waves.

NOTE: The encouragement and help given by Dr. Henry L. Viets and Dr. Laurence L. Robbins of Boston in the preparation of this manuscript are gratefully acknowledged.

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Roentgen Findings in Torulosis

Report of Four Cases[1]

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TORULOSIS IS AN uncommon disease most frequently affecting the nervous system and the lungs, and less often the liver, kidney, and spleen. Infection of the lungs alone by *Torula histolytica* is of rare occurrence. We were impressed by the infrequent incidence of this disease at the Charity Hospital of Louisiana in New Orleans, in the records of which we were able to find only 4 proved cases among 537,135 admissions in the last ten years. These 4 cases are being presented in this report.

Perhaps the first true case of *Torula histolytica* infection was described by Busse (10) in 1894. The first proved infection in the lung was in a horse, the case and the method of culturing the organism being reported by Frothingham (22) in 1902. Following Frothingham's report, Stoddard and Cutler (50), in 1916, collected and reported 10 additional cases. Their excellent and accurate description of the clinical and pathologic changes in man due to *Torula histolytica* remains little changed to the present time. In 1931, Freeman (19, 20) and Freeman and Weidman (21) collected 43 cases from the literature. In 1937, Levin (35) brought the total to 60 and, in 1941, Binford (5) increased the sum to 75. Burger and Morton (7), in 1944, reviewed the literature and added 4 cases of their own, bringing the total to 100. Swanson and Smith (52) reported 2 additional cases, and Champion de Crespigny (13) one case. This brings the recorded number of cases that we were able to find to 103. Our 4 proved cases from the Charity Hospital of Louisiana make a total of 107, as of the present date.

Torulosis is known also as European blastomycosis and Busse-Buschke's disease. The etiologic agent is *Torula histolytica* or, as it is sometimes called, *Cryptococcus neoformans*. It is a yeast-like organism belonging to the *Fungi imperfecti* and has been shown to occur normally in many types of grasses, insects, bees' nests, pickle brine, canned butter, and milk. Many non-pathogenic strains have been isolated from the throat, skin, and gastro-intestinal tract in normal, healthy individuals (8). The distribution is worldwide, cases being recorded from Germany, France, Italy, Australia, Japan, the Philippine Islands, the Dutch East Indies, Brazil, Argentina, Paraguay, and the United States.

Cultures of *Torula histolytica* do not ferment glucose (48), do not form endospores, and are best grown on Sabouraud's glucose agar, blood agar, or beef infusion glucose agar at 37° C. The organisms grow slowly (twelve hours to four days) and produce discrete, mucoid, slimy, white colonies early, which tend to become yellow to brown as they grow older (55). Microscopically the fungi appear as ovoid to spherical in shape, with thick walls, 5 to 20μ in diameter. No definite nucleus is demonstrable; however, small darkly staining bodies may frequently be seen in stained smears. The thick-walled capsule in fresh specimens may be demonstrated easily by India ink preparations. Zenker, in 1861, described an organism of yeast-like nature from a pharyngeal infection. This seems to be the first reported description of an organism of this type affecting man.

Pathologically the organisms are mainly histolytic. So great is their power that many of the inflammatory cells following ingestion of the yeast-like bodies are destroyed by them. This process is respon-

[1] From the Department of Radiology, Charity Hospital of Louisiana at New Orleans, and Tulane Medical School. Accepted for publication in July 1946.

sible for the ease of spread of the organisms to various organs.

The central nervous system is mainly affected. In 83 of the 107 recorded cases, that system alone was involved. Here the lesions may be divided into three main groups, as classified by Freeman (19–21): (*a*) meningeal, with diffuse granulomatous meningitis; (*b*) perivascular, with small granulations or cysts in the cortex; (*c*) the embolic form, with deeply placed lesions in the cortex.

Involvement of the lung by torulosis is relatively rare. Only about 20 proved cases are recorded in which the lung and central nervous system were involved at the same time, and in only 4 cases in man was the lung involved alone. In cases in which the lung is affected, the fungi apparently gain entrance through the respiratory passages. In the process of reproduction they form a nodular, gelatinous mass which is the main lesion seen grossly. The nodule or nodules are firm and are frequently of the miliary type. They often coalesce and form abscesses or cavities, particularly if secondary invaders are present. The infection may spread by the lymphatic route, but the major spread is by the blood stream. The pathologic changes occurring in the lungs as a result of infection by *Torula histolytica* are reflected on the chest roentgenogram.

The age incidence of torulosis, as reported, ranges between four and seventy years, but it is most common between the ages of thirty and sixty. Clinically the disease is characterized mainly by symptoms of meningeal irritation, an increase in intracranial pressure, and a low-grade fever. Hence, headaches, mainly frontal, occur intermittently, gradually becoming more severe and continuous. Stiffness and pain in the neck, with vertigo and dizziness, are associated. As the disease progresses, severe mental depression, disorientation, restlessness, irritability, and delirium occur. Amblyopia, strabismus, nystagmus, ptosis, diplopia, and hemiplegia are frequent later symptoms. Physical examination discloses stiffness of the neck, along with positive Kernig and Brudzinski signs. Enlarged nodes are often associated with torulosis, and, as such, may lead to confusion with Hodgkin's disease.

In cases of torulosis in which the lung is involved, a carefully taken history will usually reveal a previous respiratory infection, possibly quite mild. However, in those patients manifesting pulmonary involvement mainly, the respiratory symptoms will be severe. A bronchitis, with a cough productive of only small amounts of sputum, is typical. This form may yield a pneumonic type of infiltration in the lung, with corresponding physical findings. The easily mistaken diagnosis of tuberculous meningitis, non-specific meningitis, encephalitis, brain tumor or abscess, psychosis, or dementia paralytica is frequently made.

The laboratory findings may include a slight leukocytosis, increase in the sedimentation rate, and usually a hypochromic anemia. The spinal fluid will show an increase in pressure; it may be either clear or xanthochromic, with cells ranging from 3 to 1,000 per cu. mm., but mainly from 200 to 500. There is an increase in both the albumin and globulin fractions. The organisms may be seen in direct smears as previously described, thick-walled, ovoid, spherical bodies showing up particularly well with India ink preparations. A meningitic type gold curve is commonly obtained.

While the pathologic findings in the lungs in torulosis have been well described, we have been unable to find any representative account of the roentgen findings. One of the early roentgen descriptions of such lesions was by Berghausen (3), who, in 1927, stated that the diffuse bilateral infiltration in the lungs was not the typical picture of tuberculosis. A fluoroscopic examination of the chest of his patient showed diffuse enlargement of the nodes of the hilum and mottling of the parenchyma throughout. Sheppe (48), in 1924, had recorded a case of organizing bronchopneumonia, proved by necropsy, in which he described the chest x-rays as revealing a "nodose" involvement in the left upper

and right mid-lung field and base. The lesions in the right lung field were said to have a radial distribution not typical of tuberculosis. Taber (53) dismissed the roentgen findings as indicative of some scarring. Levin (35) reported a case in which the roentgenogram of the chest showed several fairly well defined areas of cotton-like infiltration in the left base. There was also some increase in fibrosis in the lung fields on the right, particularly in the right base. A small indefinite area of infiltration was observed, about 1 cm. in length, superimposed upon the third interspace anteriorly on the right.

We observed certain x-ray findings in cases of torulosis, which, while not pathognomonic of the disease, should strongly suggest the possibility of infection by a yeast-like organism such as *Torula histolytica*. When these findings are correlated with the clinical picture, we believe the diagnosis should be fairly certain. They were observed in all 3 of our 4 cases in which the lungs were involved. In one case, only the central nervous system was affected, while in 2 cases with lung involvement there were lesions in the central nervous system, also. One of these patients is alive three years and three months after the onset of his symptoms, while the other died in four months. Our fourth patient had pulmonary involvement alone. From the recorded medical literature it would seem that when the lung only is affected, the infection is not so nearly overwhelming as when the central nervous system is involved. This belief is borne out in our case, since the patient is asymptomatic at this time, eighteen months after the onset of his illness.

In roentgenograms reproduced in the literature, and in our own studies, we have observed that the disease has a predilection for the bases of the lungs. In 2 of our 3 cases with pulmonary involvement, the bases were first affected. In the third case the lesion when first observed was in the right second interspace. In all 3 cases, however, the early lesions presented a similar roentgen picture, and we wish to emphasize that the early lung lesions offer the most favorable opportunity for a satisfactory roentgen diagnosis of torulosis. We found these to be fairly well circumscribed patchy areas of homogeneous consolidation, with only a small amount of reaction about their edges. These small areas of consolidation tend to become confluent as the disease progresses, with or without cavity formation, and with little or no demonstrable drainage. The lesions resemble closely those of tuberculosis. However, they tend to occur more frequently in the bases of the lung, where tuberculosis is only occasionally found. As healing occurs, small amounts of fibrosis remain in the affected areas. The lymphatic structures in the hilar region may show slight enlargement, not nearly so prominent as is seen in Boeck's sarcoid and certain forms of pneumoconiosis. Then, too, the associated involvement of the nervous system present in nearly all cases of pulmonary torulosis is a strong differential point against tuberculosis.

The lung lesions as observed roentgenologically suggest a fungous infection, and, when associated with symptoms of the cerebrospinal system, should lead to the inclusion of torulosis as one of the first-choice possibilities in the diagnosis.

CASE REPORTS

CASE I: A. G., a 52-year-old colored male, first entered Charity Hospital on Oct. 6, 1943, complaining of intermittent frontal headaches, which eventually became continuous in character. The headaches followed a rather mild respiratory infection, accompanied by a slight sore throat. At first they were relieved by aspirin (5 to 10 grains), although at all times the relief was only momentary. When the patient was seen in the admitting room, the headaches had become continuous and severe, and were relieved only by opiates. A slight cough, with a mucoid sputum, was present on admission.

Inventory by systems revealed nothing of significance except a chancre, years old, for which there had been no therapy. The patient was well developed but poorly nourished and did not appear acutely ill. Positive findings on physical examination were a stiff neck and positive Kernig and Brudzinski signs.

Laboratory examination revealed strongly positive Kahn and Kline reactions. The red blood cell count was 4,130,000; white cells, 8,150 (polymor-

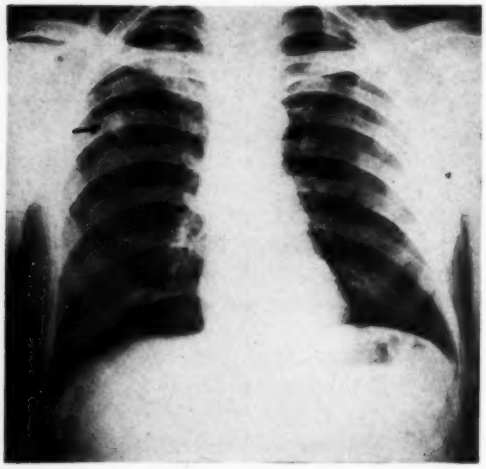

Fig. 1. Case I: A small rounded area of infiltration in the upper right second interspace. This represents a single lung lesion believed to be due to *Torula* infection.

phonuclears, 76 per cent; lymphocytes, 22 per cent; basophils, 2 per cent; monocytes, none; eosinophils, none). Urine examination was essentially negative.

A spinal tap on the day of admission revealed an initial spinal fluid pressure of 425 mm. of water and 150 cells (70 per cent polymorphonuclears and 30 per cent lymphocytes). The albumin, globulin, and total protein were increased. Sugar was decreased. On repeated spinal taps these findings were essentially unchanged. On Nov. 9, 1943, *Torula histolytica* was found in smears of the spinal fluid and cultured. Similar organisms were also obtained from the sputum. Roentgenograms of the chest (Fig. 1) revealed a fairly regular, homogeneous area of infiltration in the right second interspace. There was little or no reaction about this area and no demonstrable lymphatic drainage such as has been seen in tuberculosis.

The course of the illness continued progressively downhill and cerebral symptoms eventually occurred —dementia, disturbances in vision, paralysis of the external rectus muscles, and finally failure of the pupils to react to light.

Sulfadiazine was used in therapeutic amounts, and potassium iodide was also tried. Many spinal taps were done to keep down the cerebrospinal fluid pressure, but death occurred on Dec. 1, 1943. Autopsy was refused.

CASE II. C. C., a 24-year-old colored male, was first seen in September 1944, with an iridocyclitis and a beginning cataract. In performing a paracentesis, the lens was nicked, and several weeks later the cataract was removed. Physical and laboratory examinations were essentially negative except for strongly positive Kahn and Kline reactions. Fever therapy was given at this time.

The patient was readmitted on Feb. 11, 1945, complaining of left-sided chest pain, cough, and pain and swelling of both legs and ankles. The cough was productive of a small amount of clear, mucoid sputum.

Inventory by systems was essentially negative. Physical examination revealed some increased breath sounds in the left base and slight swelling of both ankles. There was some axillary lymphadenopathy, but apparently these lymph nodes were the only ones which were enlarged. Roentgenograms of the chest revealed fairly regular, patchy areas of consolidation in the left lower lobe which were beginning to coalesce (Fig. 2). There was some enlargement of the bronchopulmonary lymph nodes on this side, and the impression was that of an early bronchopneumonia. The patient had a low-grade fever, and a clinical diagnosis of Hodgkin's disease was made. Biopsy of an axillary node, however, revealed only adenitis with reticulum-cell hyperplasia.

At his own request, the patient was sent home several weeks later though not entirely symptom-free.

On April 8, 1945, he was readmitted, at which time he complained of a cough and pain in the left chest and in the scapular region. The cough was again productive of a white, thick sputum. There had been a loss of 10 pounds in weight in the past two months. Cough had been present intermittently since the previous admission, and the patient was more comfortable when sitting or partially reclining.

At this time the patient appeared somewhat lethargic but not acutely ill. There was some lymphadenopathy. Breath sounds were somewhat diminished in the left base posteriorly, with a few moist râles above this area. Other findings were essentially normal. Temperature was 99.4°, pulse 102, respiration 30, blood pressure 105/70.

The red blood cell count was 5,100,000; the white cell count 11,400, with an essentially normal differential count. The urine was essentially normal. Many sputum examinations and gastric washings were negative for acid-fast organisms. The electrocardiogram was normal. The sedimentation rate was 27 mm., and the Kahn and Kline reactions were now negative. Roentgenograms of the chest showed extension of the previously described areas of patchy consolidation in the left base. The discrete areas had now become confluent. Progressive films revealed extension, and finally a cavity was demonstrated (Fig. 3).

Physical examination showed some progression of signs of consolidation and fluid in the left base, confirmed by repeated roentgen-ray films. There was progression of the lung lesion, complete to consolidation in the left base, with some pleural fluid. Smears and cultures of the removed fluid revealed *Torula histolytica*, the first organisms to be detected.

The early temperature curve was of the septic type but this gradually became low-grade, running

daily from 99 to 99.4°. The patient was variously treated with sulfadiazine, penicillin, potassium iodide, gentian violet, and finally roentgen therapy. A total dose of 450 r, in air, was administered over a period of seventeen days (200 kv., 0.5 mm. Cu and 1 mm. Al filters, a half-value layer of 1 mm. Cu, 20 ma., distance of 50 cm.) through two round ports 20 cm. in diameter, centered over the lower lung fields posteriorly on each side. The plan of treatment called for a dose of 75 r (in air) three times to each of the two lung fields, one field a day alternately, for a six-day period. This could not be carried out, however, because of the patient's inability to take consecutive daily treatments, and the course was prolonged over seventeen days.

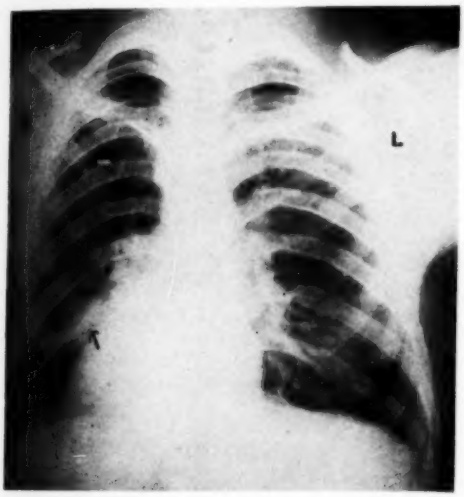

Fig. 2. Case II: Patchy areas of consolidation in the left lower lobe. See Fig. 3 for a view from the same case eight months later.

The patient was discharged on Oct. 18, 1945, at which time roentgenograms showed improvement of the lesion in the left base, as evidenced by decrease in size and the presence of some fibrosis.

The patient was readmitted on Nov. 5, 1945, with the same complaints as on his previous admission, namely, cough, chest pain, and, in addition, hemoptysis. He was again treated with sulfadiazine and potassium iodide, and left the hospital on Nov. 14, 1945. He had several more admissions, each time the chief complaints being cough and blood-streaked sputum. He was last seen on Jan. 31, 1946, when roentgen examination showed the areas of consolidation, previously observed, to be replaced by a small amount of fibrosis. There was also regression in the size of the bronchopulmonary lymph nodes in the left hilar region.

CASE III: W. T., a 25-year-old white male, was admitted because of headaches of six weeks' duration. The headaches followed a respiratory infection for which a local doctor had given some nose drops, with no relief. About three weeks after the onset of symptoms the patient experienced some spontaneous relief for three or four days, soon after which severe headaches, vomiting, and slight stiffness of the neck developed.

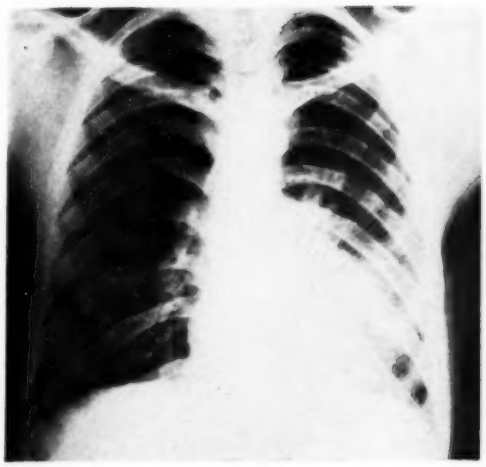

Fig. 3. Case II: The patchy areas of consolidation seen in Fig. 2, eight months earlier, have now become confluent, with cavity formation.

Upon admission to the Charity Hospital, an inventory by systems was essentially negative. On physical examination, the patient appeared well developed and well nourished, somewhat flushed and ill. Positive findings were as follows: moderately stiff neck, positive Kernig and Brudzinski signs, with a questionable Babinski sign on the right.

Red blood cells numbered 5,150,000; white cells 9,700 (polymorphonuclears 75 per cent; lymphocytes 21 per cent; monocytes 2 per cent; eosinophils 1 per cent). The urine was essentially normal and serologic tests were negative. Spinal fluid examination showed an initial pressure of 80 mm. of water, with 236 cells, and an increase in total protein as well as in the albumin and globulin fractions. There was a decrease in sugar, and no organisms were demonstrated on smears or cultures. Repeated spinal taps revealed very little difference in the findings except for some increase in the initial pressure. Repeated examinations of spinal fluid and sputum were negative for acid-fast organisms.

Roentgenograms of the chest at this time showed several homogeneous, patchy, discrete areas of consolidation in both bases, with little or no reaction about their edges (Fig. 4). Those in the left base progressed and coalesced in the course of several weeks, while those in the right cleared up with only a small amount of fibrosis remaining.

Bronchoscopy revealed nothing of significance.

During his stay in the hospital the patient had a

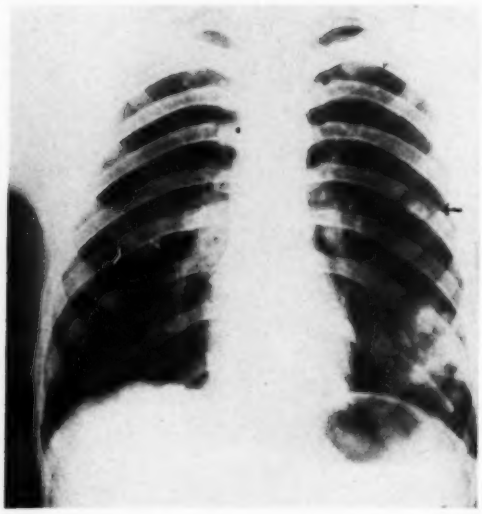

Fig. 4. Case III: Several homogeneous, discrete, patchy areas of consolidation in the left lower lobe. A single area of infiltration is observed in the left third interspace. For the same case three years later, see Fig. 5.

low-grade fever, the peak being about 99.6° F. Upon bed rest and adequate diet, with high vitamin supplements, he improved and left the hospital on March 18, 1943. The sole diagnosis was meningitis.

After leaving Charity Hospital, the patient went to the Mayo Clinic. There *Torula histolytica* was obtained from smears and cultured from both the spinal fluid and the material obtained from a bronchoscopic examination. Tyrocidin was given intrathecally, with little effect. The patient was then given 45 grains of sulfathiazole daily for several weeks and sent home. There was some improvement in his headaches, but because of some gastro-intestinal disorder he stopped taking the drug. Since then he has been followed in the out-patient clinic here, with several admissions to the hospital, upon which occasions the organisms have been found in the spinal fluid, both on smears and cultures. He has received 7,000,000 units of penicillin and some intrathecally, with no apparent effect.

The residual findings are: bilaterally increased deep tendon reflexes in both lower extremities, an unsustained bilateral ankle clonus, an increase in spinal fluid protein, with a decrease in sugar. The patient has been working part time and getting along well except for occasional severe headaches (three years and three months following the onset of symptoms). The most recent roentgenogram of the chest showed the lesions at both bases to have cleared up, leaving only a small amount of fibrosis (Fig. 5).

CASE IV (in this case there were no pulmonary findings): E. M., a 6-year-old colored male, was admitted to the hospital on April 14, 1945, having had, for two weeks, a mild respiratory infection, accompanied by vomiting several times, loss of appetite, and sore throat. On the day of admission the boy complained of a frontal headache and stomachache, and on this day he had a convulsion.

He was a normally developed child, with a birth weight of 5 pounds 12 ounces. He appeared poorly nourished and somewhat lethargic. Positive findings included enlarged and injected tonsils, some enlarged submaxillary lymph nodes, a stiff neck, and positive Kernig and Brudzinski signs. The red blood cell

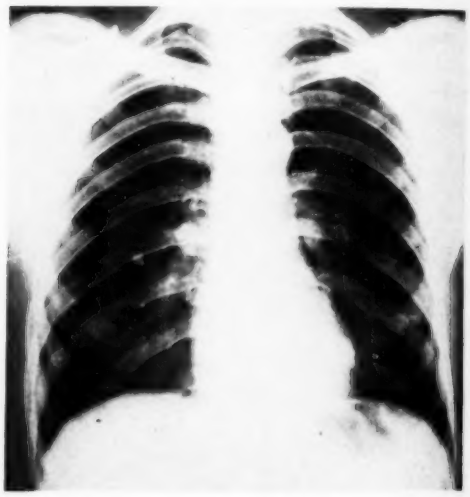

Fig. 5. Case III: The areas of consolidation seen in Fig. 4, three years earlier, have disappeared and are replaced by fibrosis.

count was 4,500,000; white cell count 13,120 (525 polymorphonuclears; lymphocytes 46 per cent; monocytes 4 per cent). The urine was essentially negative.

The spinal fluid was clear with a pressure of 104 mm. of water. There were 300 cells on the first tap, and this level was maintained on succeeding examinations. The Pandy reaction was 2 plus, and both albumin and globulin fractions were increased; sugar was normal. Roentgenograms of the chest were negative. Smears and cultures of the spinal fluid on Sabouraud's medium revealed the typical *Torula histolytica*. Injection of the fluid into a rat killed the animal in three days.

The patient was given intrathecal penicillin, sulfadiazine, and potassium iodide, but in spite of all medication he died on June 13, 1945. Autopsy was refused.

SUMMARY

1. Torulosis is an uncommon disease. Only 4 cases were found in 537,135 admissions to the Charity Hospital of Louisiana in New Orleans during a ten-year period.

2. When the lungs are involved, roentgenograms made in the early stage reveal small, circumscribed, patchy areas of consolidation which have a tendency to become confluent, with or without cavity formation.

3. The bases of the lungs are most often affected by the disease.

4. When healing occurs, it is by fibrosis.

5. In one of the 4 proved cases recorded here, the lung lesion was single. It would appear that torulosis of the lung may be single, but most often is multiple.

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A Study of 24,615 Separation Chest Roentgenograms[1]

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Major, Medical Corps, Reserve

Discussion of chest x-ray and allied surveys of military personnel have stressed the importance of routine preinduction and separation examinations to the taxpayer, the soldier, and the public health. These reports all look forward with interest to the next step—the post-war separation examinations. The results of such an examination are offered here. While previous surveys, by their nature, were only local in scope, the present study represents a greater geographic and economic cross-section, since the separatees are the entire output of an Air Force Auxiliary Separation Base. They are natives of every state in the nation, ranging in rank from colonel to private, representing virtually every nationality and race. The ages are from 18 to 44 years; those whose separation was deferred because of chest abnormalities are all in the 18 to 25-year group. No attempt is made to distinguish racial incidences—first, because of a technical difficulty; second, because the environment in the Army was the same for all races. Fourteen- by seventeen-inch, double emulsion, high-speed x-ray film was used and re-examinations, including fluoroscopic, lordotic, and stereoscopic technics, were employed when indicated.

The findings on separation (Tables I–IV) are quite consistent with those on the induction examination, save for an expected increase in the number of intrathoracic metallic foreign bodies and a decreased incidence of active tuberculosis. As might be expected after the thorough screening at induction and the close medical observation of most Air Force personnel, both active and apparently healed tuberculous lesions are comparatively few (Table I). Differences between enlisted and commissioned personnel were insignificant. Although many of the diagnoses were confirmed clinically or in the laboratory, most were based on the commonly accepted roentgen criteria. The classification used in Table I is that recommended by the National Tuberculosis Association with the exceptions noted. Five of the minimal tuberculous lesions of undetermined activity are still under observation. One patient with right upper lobe atelectasis was thought to have a bronchiogenic tumor until the bronchoscopist reported tuberculosis of the bronchus. All patients

Table I: Comparative Study of Tuberculosis Before, During, and After Army Service

	Separation Series		Rate per 1000 in Other Series			
	Cases	Rate per 1000	Series 5 (Fine and Steinhausen)	Series 6 (Kinzer)	Series 2 (Brown)	Series 7 (Levitin)
Advanced tuberculosis	2	0.0812	0.03	0.14		
Moderately advanced tuberculosis	10	0.406	0.19	0.6		
Minimal tuberculosis	10	0.406	1.41	5.0		
Undetermined activity	5	0.203	0.44			
Arrested tuberculosis of minimal extent, not considered clinically significant (10)	903	36.6	1.44			
Miliary calcifications	8	0.324	0.34			
Tuberculosis of bronchus	1	0.04				
Total Active Tuberculosis	27	1.09	2.06	9.5	6.2	7.1

[1] From the Department of Radiology, Southwestern Medical College, Dallas, Texas. Accepted for publication in May 1946.

TABLE II: OTHER DISEASES OF LUNG AND PLEURA

	Cases	Rate per 1000	Rate per 1000 in Other Series*	
Primary atypical pneumonia	15	0.60	0.45	(6)
Pneumothorax (spontaneous)	5	0.203	0.25	(1)
Bullous emphysema	4	0.16	0.16	(6)
Bronchiectasis (probable)	4	0.16	0.8	(6)
Boeck's sarcoid	1	0.04		
Pneumoconiosis	1	0.04	0.11	(2)
Lobectomy	1	0.04	0.019	(6)
Atelectasis due to tuberculosis of bronchus	1	0.04		

* Figures in parentheses in this and following tables refer to Bibliography.

TABLE III: DISEASES OF THE HEART, MEDIASTINUM, AND DIAPHRAGM

	Cases	Rate per 1000	Rate per 1000 in Other Series	
Cardiac enlargement	27	1.09	5.2	(6)
Wide ascending aorta	5	0.203		
Mediastinal masses	5	0.20	0.2	(2)
Large epicardial fat pad	3	0.121		
Hepatic masses (clinical history of amebiasis)	3	0.121		
Dextrocardia	2	0.0812	0.3	(1)
Right-sided aorta	1	0.04		
Eventration of diaphragm	1	0.04	0.085	(6)
Herniation of diaphragm	1	0.04	0.1	(2)

TABLE IV: SKELETAL DISEASES AND ABNORMALITIES

	Cases	Rate per 1000	Rate per 1000 in Other Series	
Cervical ribs	14	0.57	1.7	(4)
Resected ribs	10	0.406	0.8	(4)
Scoliosis (over 2 cm.)	7	0.27	3.1	(4)
Compression of dorsal spine	4	0.16		
Traumatic arthritis of dorsal spine	2	0.0812		
Cervical spina bifida	3	0.121	0.085	(6)
Cystic defect of ribs with peripheral sclerosis	2	0.0812		
Apparent non-union of fractured clavicle	2	0.0812		
Acromioclavicular separation	2	0.0812		
Calcification of shoulder bursae	2	0.0812		
Osteoma of scapula	2	0.0812		
Multiple exostosis of ribs	1	0.4		
Miscellaneous				
Foreign bodies	8	0.324	0.1	(2)
Aerocele of larynx	2	0.0812		

having active tuberculous lesions (confirmed clinically and in the laboratory) or any communicable disease were transferred to a nearby Regional Hospital and separation was deferred.

Table II lists the diseases of the lungs and pleura discovered, other than tuberculosis. The presumptive roentgen diagnosis of bronchiectasis was made on the routine chest film. In one case there was residual lipiodol. No confirmation has been received on the other three cases. The one case of pneumoconiosis is not a classical example. The peribronchial lymphatic chains were clearly outlined in calcific density but were not swollen or enlarged, and the parenchyma was essentially normal. Those men found to have primary atypical pneumonia and spontaneous pneumothorax allegedly had no symptoms. It is believed that complaints were suppressed in many cases in the fear that medical care would postpone or prevent separation. Diseases of the heart, mediastinum and diaphragm discovered in the course of the survey are listed in Table III, and skeletal diseases and abnormalities in Table IV.

Of the 24,615 men examined 23,537 were considered to have "no significant abnormality," a phrase advised by War Department Directive (10). "Significant abnormalities" in our opinion do not include simple tenting of the diaphragm, mild scoliosis, bifurcations or pseudarthroses of the ribs, azygos veins, fibrotic apical caps, or a few discrete, well calcified nodules in the hilus or parenchyma of the lung. One other term suggested by higher authority (10), to be used with care, was "arrested tuberculosis of minimal extent not considered clinically significant."

A comparative study of significant chest x-ray abnormalities in other surveys is included in the tabulations of findings on separation from service. The source of the figures given for comparison are indicated by the series number and name at the top of each column. Series 5 is a survey of 32,000 soldier candidates for aviation cadet training; others are of pre-induction examinations.

DISCUSSION

The percentage of men examined for separation at this field exhibiting active or questionably active tuberculosis—0.1 per cent—compares favorably with pre-induction surveys, which usually showed over 1.0 per cent active tuberculosis. Whether these men came into contact with and developed tuberculosis while in the service or whether old, apparently quiescent foci were relighted is a question worthy of investigation. The fact that none of the active lesions observed was of the primary type, and the fact that some of the men examined had never had pre-induction chest roentgenograms, may be considered as evidence that the disease was not acquired in the Army. None of the patients exhibiting active lesions had miliary calcifications in the parenchyma. Rigorous periods of combat and training, on the other hand, were experienced by many of the men with active lesions and may have served to cause recrudescences. These questions can better be studied at the General Hospitals to which the active cases have been transferred. There the pre-induction and subsequent roentgenograms may be compared and more time will be available to evaluate the medical history of each patient.

SUMMARY AND CONCLUSIONS

1. The significant abnormalities found in 24,615 chest roentgenograms made upon separation from Army service are tabulated and compared with pre-induction surveys.

2. The incidence of active tuberculosis, although significantly lower than on pre-induction examination (average over 1.0 per cent), is still higher than might be expected (0.1 per cent).

3. The incidence of other abnormalities of the chest is almost identical with that found on previous surveys.

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Aortic Aneurysm Secondary to Coarctation

Report of a Case Showing Calcification[1]

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ANEURYSM OF the descending aorta secondary to coarctation of the aorta has been reported frequently in the literature. This paper is not intended to cover exhaustively the problem of aortic coarctation; it does propose, however, to stress the radiographic diagnosis, not only by such conventional features as absence of the aortic knob, left ventricular enlargement, and rib notching, but also by the unusual finding of calcified ring shadows in the region of the aortic arch. In the case presented below, these ring shadows were not at first thought to be associated with the coarctation; subsequently, however, they were found to be areas of calcification in aneurysmal dilatations of the aorta below the coarctation.

Mrs. B. S., a 25-year-old housewife, was first seen in the Out-Patient Department of the Buffalo General Hospital in March 1944, with diabetes, which she was known to have had since 1942. There was no history of illness referable to the cardiovascular system.

Physical examination revealed the following pertinent findings:

Heart: The apex impulse was 2.0 cm. outside the mid-clavicular line in the 7th intercostal space; there were no thrills; the character of the pulse was good, regular, and of pronounced intensity. The second aortic sound was greater than the second pulmonic sound. The blood pressure was 140/180.

Lungs: Resonance was equal on percussion. Inspiratory râles were heard in the left bronchial area anteriorly, also posttussic râles in the left mid-chest.

Laboratory Studies: The urine was acid, negative for albumin, and positive for glucose; a smear showed few red blood cells and many white blood cells. Blood glucose was 119–279 mg. per cent. Serologic tests were negative.

Roentgen Studies: Fluoroscopic and radiographic examination of the chest showed four calcified ring shadows in the posterior mediastinum at about the level of the aortic arch, varying from 1.75 to 5.0 cm. in diameter (Fig. 1). These areas were non-expansible, and it was thought that the pulsations were transmitted from the aorta. In addition, the aortic knob was absent and the eighth rib on the left and the seventh and eighth on the right showed slight notching of their inferior surfaces posteriorly (Fig. 1, A). The impression was coarctation of the aorta. The significance of the calcified ring shadows was not determined.

Course: The patient became pregnant and on Jan. 4, 1945, entered the Buffalo Children's Hospital, at term. Cesarean section was done on Jan. 5, in view of the complications of diabetes and hypertension (blood pressure was 150/100 at this time). The immediate postoperative course was uneventful. On Jan. 16, however, the patient began having chills, and her temperature rose to 103–104°. The abdomen was diffusely tender, especially in the right lower quadrant. Penicillin was administered intramuscularly, and transfusions of whole blood were given but the temperature again spiked to 102°. Physical examination revealed a mass in the right lower quadrant of the abdomen. An exploratory laparotomy was done on Jan. 25; an abscess in the right broad ligament was drained, and sulfathiazole powder was dusted into the wound.

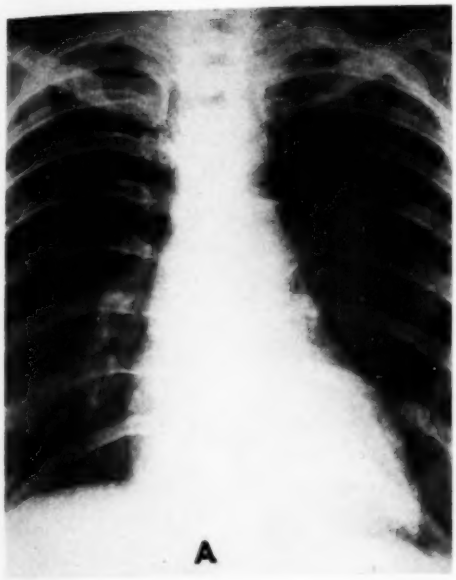
The patient improved until Jan. 31, when the temperature again rose to 102°. She became cyanotic, respirations were rapid and shallow, and on Feb. 1, she became comatose. Death occurred the following day. The terminal temperature was 107°.

Laboratory Findings: The urine was positive for sugar, and occasionally positive for albumin, white blood cells, and urates. Blood glucose was 43–248 mg. per cent. A portable chest film[2] again showed the calcified oval ring shadows in the region of the aortic arch, also the rib notchings. The lungs were clear.

Necropsy: The postmortem examination (Dr. Kornel Terplan) was restricted to the abdominal cavity and the thorax. For this reason, no dissection of the branches of the subclavian arteries was possible. Only the findings relative to the thoracic aorta, which were entirely incidental, will be given. The cause of death actually was a diffuse purulent peritonitis with subdiaphragmatic abscesses following purulent inflammation of the wall of the uterus and a fetid abscess in the right tubal angle several

[1] From the Department of Radiology, Buffalo General Hospital, Buffalo, N. Y. Accepted for publication in July 1946.

[2] The authors wish to express their appreciation to Dr. G. Newton Scatchard of the Buffalo Children's Hospital for the privilege of viewing this film.



ous upper part of the descending thoracic aorta showed considerable aneurysmal dilatation, forming a solid, unusually firm protrusion along the medial contour of the vessel. The wall of this protrusion appeared calcified to the palpating finger. The aneurysmal sac was completely filled by firmly thrombosed blood. Only the left subclavian artery appeared moderately dilated; the other arteries, including the innominate artery, the right subclavian, and both carotid arteries, appeared of normal caliber (they were cut just at the exit from the aorta). When the descending aorta was opened, it could be seen that the intercostal arteries going off the thoracic aorta, especially the upper two pairs and in particular those on the left side, were of distinctly greater caliber than normal. The uppermost, immediately distal to the stenosis, measured 4.0 mm. in diameter.

The drawings by Mr. Melford Diedrick, reproduced in Figures 2 and 3, show very clearly the relationship of the aneurysm to the aorta.

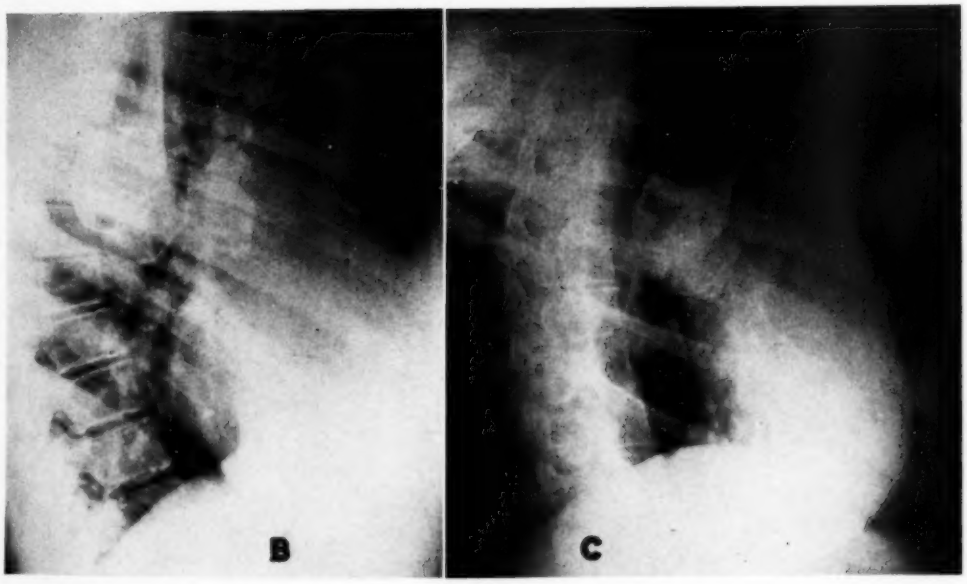


Fig. 1. Postero-anterior, lateral, and oblique views of case of Mrs. B. S. Rib notching and calcification in the aneurysmal wall can be recognized.

weeks after cesarean section. There was also some serous and purulent exudate in both pleural cavities and atelectasis with some inflammatory edema in both lungs.

Dissection of the aorta revealed extreme stenosis of the arch corresponding to or slightly below the level of the isthmic portion. The directly contigu-

We have recently seen another case of coarctation of the aorta in a white male, age 42 years, whose chief complaints were aching legs and chest pain. His films showed certain interesting features which we believe merit mentioning. First is the multiplicity of rib notchings. The 3d to the 9th ribs bilaterally showed multiple

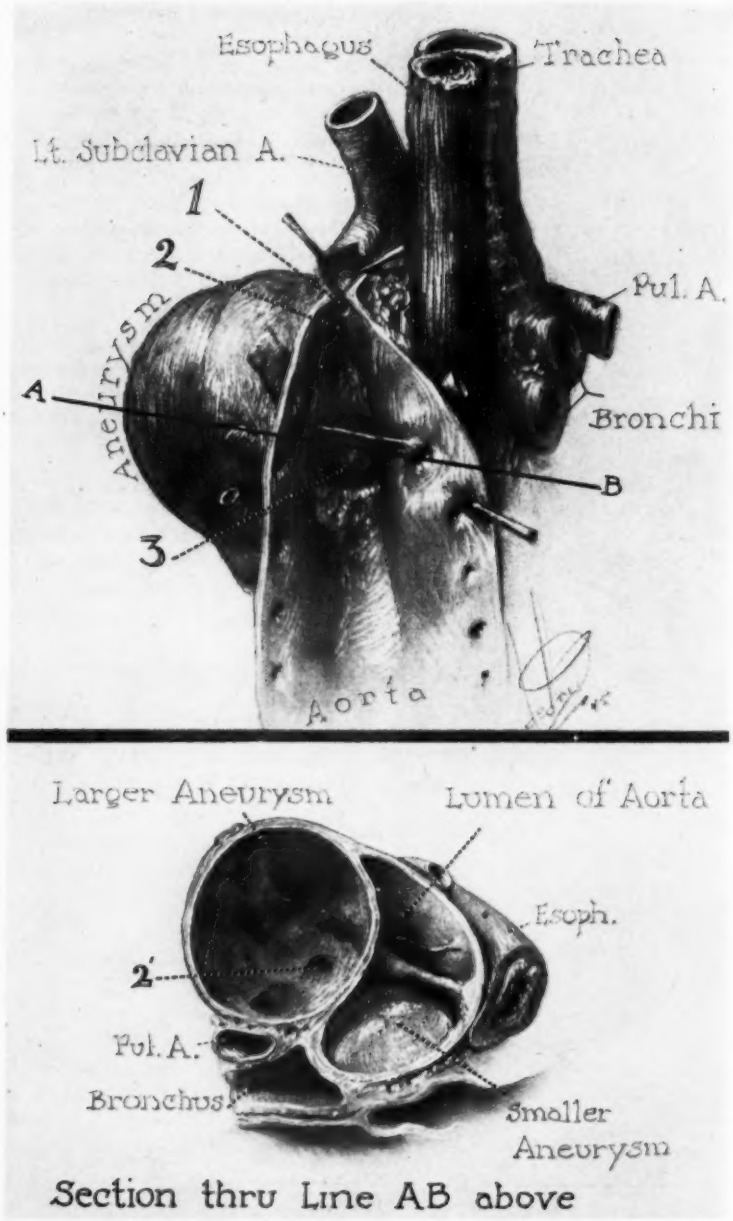


Fig. 2. Posterior view of the specimen after heart and lungs were removed and the descending portion of the thoracic aorta was opened. 1. Marked stenosis of isthmus. 2. Distinct erosion in the wall of the thoracic aorta, caused by pressure from the upper portion of the sac where the aneurysm is secondarily corroding the aortic wall from without. 3. Opening leading into the aneurysmal sac. The short tendon-like bridge crossing over this opening is apparently the last remnant of the intimal and subintimal tissue at the site where the aneurysm was formed. It is obvious that the aneurysm had formed in a medial and somewhat anterior direction. Note also the large caliber of the upper three branches of the intercostal arteries.

Fig. 3. Section along the line A-B in Fig. 2, in a fairly transverse plane with the upper segment of the aneurysm and the aorta. The firm calcification in the wall of the aneurysm is clearly seen. The largely organized, firm, thrombosed material has fallen out, exposing the uneven, somewhat shrunken, firm plaques in the calcified wall of the aneurysm. 2′ corresponds to the point of erosion denoted by 2 in Fig. 2.

notchings of the inferior surfaces posteriorly (Fig. 4, A). This generally conforms to the finding of Bramwell and Jones, who in their series of cases noted that the notches were commonly confined to the ribs between the 3d and 9th, and absent in the first two and last three. It has been shown by these authors and by Wolke, whom they quote, that notching is due to tortuosities of the intercostal arteries as a result of the collateral circulation. The first two intercostals arise above the coarctation, from the subclavian by the superior intercostal. Except for giving off large branches near their origin, which anastomose with the aortic intercostals, they play no part in the collateral circulation and do not become tortuous (Bramwell and Jones). The shorter collateral channels to the upper aortic intercostals naturally enlarge first, and this, according to these authors, is probably why notching seldom extends below the ninth rib.

The second feature is the presence of a fusiform, soft-tissue density just distal to the coarctation, as seen in the left anterior oblique projection (outlined by arrows in Figure 4, B). This is interpreted as an aneurysm of the descending aorta, distal to the coarctation. Also to be noted is the absence of aortic shadow proximal to this soft-tissue density. Figure 4, C, is a postero-anterior projection and shows absence of the aortic knob.

DISCUSSION

Roesler classifies aortic aneurysms according to their etiology as follows: (1) embolic or mycotic; (2) arteriosclerotic; (3) rheumatic; (4) syphilitic; (5) due to coarctation of the aorta. Aneurysms proximal to the point of stenosis occur relatively frequently (Abbott), and their etiology is apparent; however, until one appreciates the collateral circulation thereby established, aneurysmal dilatation *distal* to the coarctation may at first present an etiological problem.

Bramwell and Jones beautifully demonstrated the collateral circulation by taking a series of roentgenograms during the injection of barium paste into the common carotid artery of a cadaver known to have had coarctation of the aorta. They concluded that there are four routes by which the blood can reach the aorta beyond the coarctation. These collateral channels they term: (1) *scapular and cervical*, in which the transverse scapular and transverse cervical, the posterior scapular and superficial cervical, and the long thoracic and subscapular arteries form an anastomotic network with the lateral and dorsal branches of the aortic intercostals; (2) *internal mammary*, in which the superior epigastric, the musculophrenic, the mediastinal branches and aortic intercostals anastomose with the deep epigastric branches of the internal iliac, phrenic branches of the thoracic and abdominal aorta, and terminal branches of the aortic intercostals, respectively; (3) *intercostal*, in which the terminal, lateral, and dorsal intercostal branches, and the first and second intercostals anastomose with the intercostal branches of the internal mammary artery, the subscapular and long thoracic arteries, the posterior scapular and the upper aortic intercostals, respectively, together with anastomoses between each intercostal with those above and below; finally (4) *spinal*, in which the spinal artery, being reinforced by blood from the vertebral artery, pours blood into the spinal branches of the aortic intercostals, and branches of the inferior thyroid artery join the spinal arteries.

Abbott has stated that in certain cases there is frequently a bulbous dilatation of the aorta immediately below the constriction. According to her, the dilatation may be so marked as to constitute a true saccular or fusiform aneurysm. This is accounted for by the influx of returned blood at this point where the three upper aortic intercostals are given off.

Nicolson described a case of coarctation of the aorta in a child with arrested subacute bacterial endocarditis, and a calcified mycotic aneurysm at the seat of the stricture. She believes that mycotic aneurysms are found commonly immediately

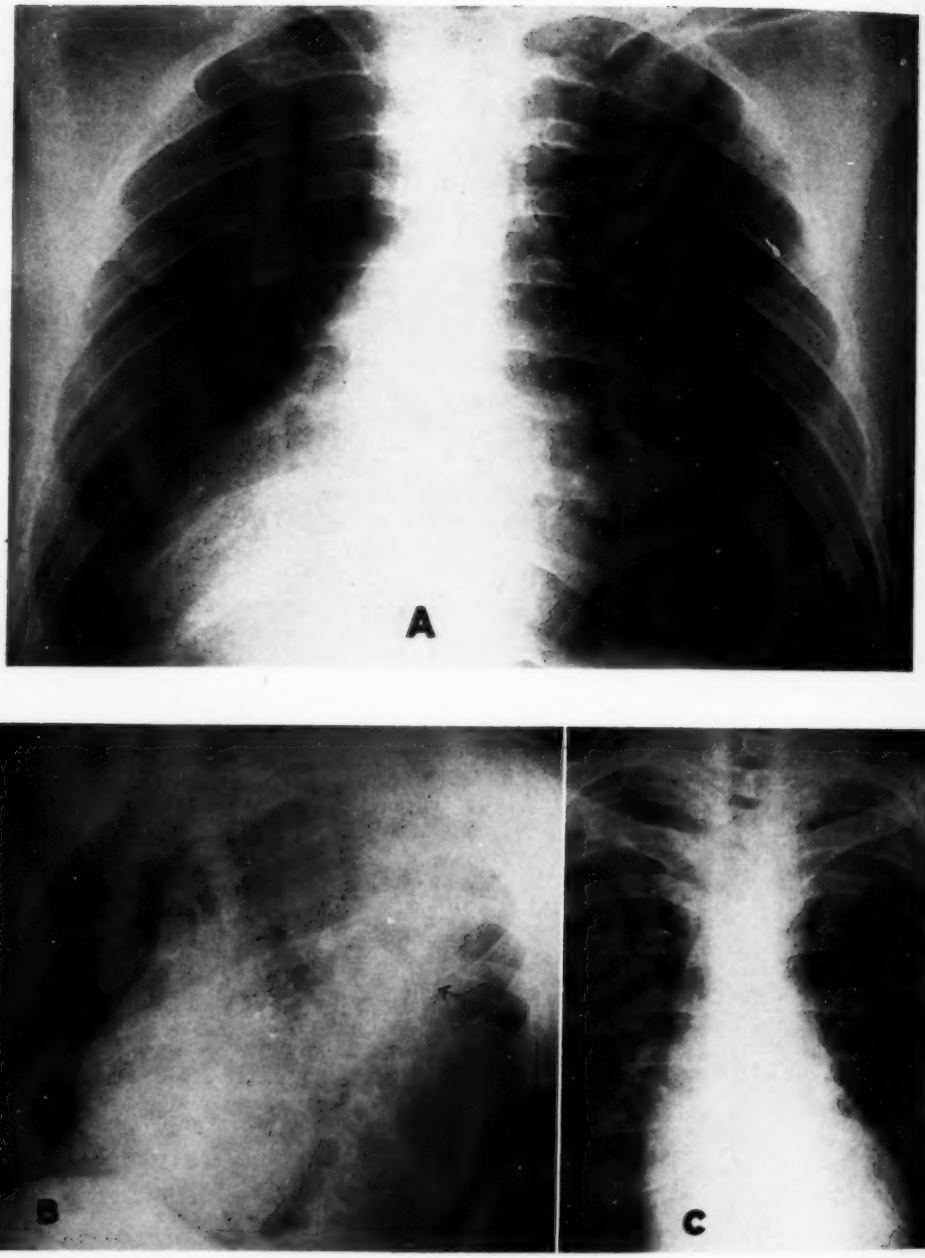


Fig. 4. Views of second case. Marked rib notching and absence of the aortic knob can be seen in the postero-anterior view. Aneurysmal dilatation is marked by arrows in B.

distal to the point of narrowing because of kinking and wrinkling of the aorta secondary to the eddying currents here. This is likewise the belief of Zaslow and Krasnoff, who report a case of aneurysm of the aorta distal to a coarctation with rupture in a 25-year-old white male. In Abbott's experience, rupture distal to the coarctation occurs less frequently than rupture proximal to the coarctation.

The establishment of eddying currents immediately distal to the coarctation apparently predisposes to superadded infection in this region from micro-organisms circulating in the blood stream (*Streptococcus viridans;* rarely, also, pneumococci). This results in the formation of a so-called mycotic aneurysm. Abbott believes that mycotic aneurysms are a "grave danger" that attend the presence of the adult type of coarctation.

It would seem that the majority of aneurysms distal to the stenosis are formed directly as a result of the collateral circulation secondary to the coarctation and are not related to infection.

SUMMARY

1. A case of coarctation of the aorta, including the postmortem findings, is presented, which radiographically showed calcified ring shadows in the region of the aortic arch.

2. Certain interesting radiographic features of a second case are discussed.

3. The collateral circulation attending coarctation of the aorta is presented.

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Problems of Acquired Radioresistance of Cancer: Adaptation of Tumor Cells[1]

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EXPERIENCE shows that malignant tumors of various microscopic structure which respond to initial irradiation may lose their radiosensitivity in part or whole during or after radiation therapy. Thus, they acquire various degrees of radioresistance, which, in the opinion of many observers, is one of the main causes of failure of radiation therapy.

Little is known of the causes of this interesting and obviously important phenomenon. Ferroux, Regaud, and Samssanow (10), in experimental studies, found no demonstrable structural changes associated with decreased radiosensitivity of tumors. The various opinions in this field (2, 3, 13, 20, 21, 23) may be summarized as follows:

1. According to one theory, there is a certain selection of tumor cells present during the course of the first irradiation. The more sensitive cells become disintegrated and the more resistant ones retain their vitality. It has been assumed that each tumor consists of a conglomerate of resistant and sensitive cells which cannot be differentiated microscopically. The resistant cells are not destroyed in the course of irradiation and they are the seed for the growth of a new, more resistant cell strain (10, 23).

2. The hypothesis of induction, by irradiation, of a biological mutation of the cancer cells, *i.e.*, a change in their "character," was advanced as early as 1905 (24). It has been stated, for instance, that an alveolar cancer of the breast became scirrhous after roentgen irradiation. This theory has had many followers, and the belief has been repeatedly expressed that after irradiation a new type of radioresistant cell may develop (20).

3. According to still another view, a functional change affects the connective tissue in which the neoplastic cells are embedded. Injured by irradiation, this no longer reacts to the presence of the tumor and no longer hinders the relentless growth of tumor cells (13). A number of investigators (16, 17, 18) believe that connective-tissue damage by irradiation may be present even though no microscopic signs of retrogressive changes are observed.

The phenomenon of radiologic induction of biological mutations has been attributed by early French authors to a common property of the radiant energy, namely, that of producing more highly differentiated structures from anaplastic and less highly differentiated tissues (*maturation évolutive*). Increased cornification of the epithelium of the skin and transformation of squamous epithelium of mucous membranes into excessively cornified epithelium after irradiation are well known.

The microscopic demonstration of the development of cornified structures, following irradiation, in basal-cell cancers (23), which as a rule do not cornify, substantiates this theory to a certain extent. I have had frequent opportunities to corroborate these observations. Cathie (3), who also described keratinization and transformation of basal-cell tumors into prickle-cell structures, stated that with this change of structure, the sensitivity of basal-cell cancers decreases correspondingly to the level of squamous-cell cancers. Newell (15) doubts, however, that such a difference in sensitivity exists.

The observations which enable me to express an opinion of the causes of acquired radioresistance of tumor cells on a cyto-

[1] From the Department of Radiology, Stanford University School of Medicine, San Francisco, Calif. The last of a series of four papers accepted for publication in June 1946.

physiological basis were made on the epithelium of the human larynx irradiated for cancer (27). They can be briefly summarized: In the *first phase* of irradiation, at the height of fibrinous reaction, the cells of the epithelium are entirely destroyed. In the *second phase*, the epithelium is regenerated but is metaplastic, revealing epidermoid and markedly cornified structures. In the *third phase*, the epithelium, as a rule, becomes atrophic; advanced squamous metaplasia persists in those cases in which the subepithelial connective tissue has undergone hyaline sclerotic transformation. If excessive doses are administered, ulcerations develop. These remain superficial if the subepithelial connective tissue is not transformed as described above. In 2 out of 10 cases, the newly formed metaplastic epithelium exhibits a definite tendency toward atypical growth into the depth of the connective tissue. In these instances no changes of connective structures are evident.[2]

From a radiobiological point of view, cornified squamous epithelium must be considered in relation to the original epithelium as a functionally more highly differentiated and, therefore, more radioresistant tissue (see above). If a new cancer develops from such highly differentiated metaplastic epithelium which has proliferated during irradiation, this cancer is likely to be more resistant to irradiation than the original tumor developing from the non-irradiated and less differentiated structures.

In the past, observations made it reasonable to believe that basic changes in morphology and radiobiology of the epithelium could be successfully compared with neoplastic proliferations of this tissue, namely with malignant squamous or transitional-cell or basal-cell tumors (1, 4, 17, 18). The epithelium may therefore be considered a suitable test object for the study of biological changes which take place in epithelial cancer during and after irradiation.

In comparison with the cyclic alterations in the epithelium, it becomes conceivable that alternating changes of destruction and regeneration take place within the irradiated tumor and that these are associated with cellular metaplasia. The final results of this are as follows: (*a*) progressive atrophy of changing cell generations, with final disintegration of the tumor and clinical cure; or (*b*) development of a more highly differentiated, radioresistant cell strain associated with clinical arrest of growth and presence of a "residual" tumor; or (*c*) formation of a new cancer from the radioresistant cell structures, first in the tumor bed itself and later in adjacent structures, and clinical progress of the tumor growth.

We do not possess microscopic criteria which would indicate the final degree of radiosensitivity of the tumor cells as related to the susceptibility of the primary cell structures. Due to the close proximity of cells of different age, vitality, morphology, and degree of differentiation in the same tumor, the different phases of cellular metaplasia and radiobiological metamorphosis cannot be followed in the cancer as they can in microscopic studies of the epithelium of the larynx or in simple experiments. An exception is the cornification of squamous-cell and basal-cell tumors.

In the epidermis, cell regeneration occurs during or after protracted fractionated irradiation from cells of the basal layer, which are considered to possess greater radiosensitivity than more highly differentiated structures of the epithelium. Consequently, in order to understand the continuous proliferation of epithelial tissue from this germinative layer, in view of its maximal radiosensitivity, we must assume that parts of this layer become adapted early to radiant energy and maintain their reproductive capacity.

In connection with this observation, it is likely that regeneration of tumor cells

[2] Generally, the regenerated epithelium of the larynx exhibits a tendency to atypical growth in the presence of chronic inflammatory changes in the subepithelial connective tissue. These develop in the larynx, chiefly in cases of chronic tuberculosis. Goldzieher described precancerous epithelium of the larynx after diphtheria, also.

takes place during and after irradiation from germinative cells which are not necessarily residuals of primarily resistant elements. It is more probable that they develop from cells which, from generation to generation, increasingly adapt themselves to radiant energy and to nutritive conditions produced by irradiation in the environment of the tumor. Their sensitive biological phases, the mitoses, may take place during the after effects of irradiation on structures surrounding the cells; therefore, a new cell strain may arise which, while still *in statu nascendi*, is exposed to the direct or indirect influences of radiant energy, to which it subsequently adapts itself.

I propose to define the adaptability of tumor cells as their property of changing their metabolic requirements in consecutive cell generations, according to prevailing conditions. The latter may differ considerably from those present at the place and time of origin of the tumor. They may include spontaneous variations of the biological *milieu* if the tumor invades heterotopic tissues, as well as pathological changes induced by radiant energy in the surrounding structures.

Little is known concerning the adaptability of tumor cells except its effects as indicated by the basic ability of malignant tumor cells to grow and to reproduce in a tissue entirely different from the primary stroma (heterotopic growth). The process of adaptation, therefore, is unrelated to the phenomenon of recovery of irradiated tissues, with which it has been repeatedly confused. The inherent potentialities of normal epithelial cells to adaptation are exhibited in their property of producing metaplasias.

Not only the faculty of malignant tumors to grow heterotopically, but also their capacity to form metastases, favors the conception of adaptation. Emboli of tumor cells in lungs and liver are quite frequent in the presence of a primary malignant tumor. Most of these emboli become disintegrated without forming metastases. Only those cells will produce metastatic foci which are able to adapt their metabolism to conditions prevailing at the site of their innidiation. Moreover, it has recently been shown that the frequency of formation of remote metastases is in direct relation to the ability of the tumor to form discontinuous local metastases in the vicinity of the primary focus. This can be comprehended only when it is considered that extension into heterotopic tissue or formation of local discontinuous metastases not only indicates the powers of the tumor for adaptation but shows that some cells are already adapted to the changed environment. These cells are more likely to survive not only in tissues in the immediate vicinity of the tumor but also in distant organs such as lymph nodes, liver, lungs, etc. Hence, these are the cells which most frequently become the matrix of metastases. In this connection it is worth while mentioning that occasionally basal-cell cancers appear in metastases as squamous, cornifying carcinomas.

Another factor often considered as decisive in the development of remote metastases, namely, the general deterioration of the host, could not explain why in many instances early metastases are produced by relatively small tumors, for instance small gastric carcinomas, prior to the presence of clinical signs of deterioration of the patient. A sudden spread of metastases in the terminal stages could be explained by accentuation of the effects of adaptation through decreased resistance of tissues of the host.

There are many indications that when a tumor cell adapts its metabolism to a heterologous tissue, it simultaneously adapts its radiosensitivity as well. Whether this is due to the presence of a common factor simultaneously influencing cellular metabolism and specific radiosensitivity or whether the change of radiosensitivity follows alterations of metabolism cannot be decided from our studies. It seems, however, that the capacity of the tumor cells to adapt themselves to one vicissitude is persistently correlated with the capacity to adapt to another. Close

relationship between intensity of metabolistic activity of cells and their radiosensitivity is an established fact. In this connection the following generalizations may be enumerated:

1. Any tumor reveals decreased radiosensitivity if it invades different tissues from those surrounding it at its place of origin. For instance, a squamous-cell tumor becomes less sensitive if it grows into cartilage, muscle, fat, bones, or into connective tissue, functionally different from its original environment.

2. Metastatic growths are, as a rule, less sensitive than the primary tumor.

3. If diffuse irradiation is used, the same focus of tumor growth (alveolus) is more resistant in its peripheral portions, where its metabolism is adapted to the surrounding connective tissue, than in the central portion, where it often exhibits signs of spontaneous retrogression.

4. Tumors which possess an abundance of connective-tissue stroma adapt their metabolism to nutritive conditions provided for them by the excess of collagenous tissue, which is highly radioresistant. The simultaneous change in their radiosensitivity explains why a scirrhous adenocarcinoma, for instance, is less sensitive than a solid alveolar adenocarcinoma.

5. Epithelial tumors which do not have the intrinsic ability to develop more highly differentiated and consequently more resistant strains, such as many anaplastic tumors, are apt to retain their radiosensitivity as long as they remain localized in the tissue of their origin. However, if they have the capacity to adapt themselves to surrounding tissues and invade adjacent heterologous structures, they become more or less resistant to irradiation. A good example is the behavior of anaplastic cancer of the cervix, the sensitivity of which is considerably decreased if it invades, for instance, the adjacent wall of the vagina. The experience in such cases cannot be vitiated by restriction of the physical dose, as it is in some other situations. The vaginal wall is accessible to the very same dose which is delivered at the cervix itself.

The author adds the following conclusions from his experience:

During radiation therapy, the connective stroma is included in the irradiation and often becomes replaced by structures whose radiosensitivity is much lower than that of the primary non-irradiated connective tissue. Consequently, if tumor cells regenerate after primary injury by radiation, the new cell strain must be considered as being, to a certain extent, already adapted not only to the radiation, but simultaneously to nutritive values of connective stroma which itself has changed under the influence of radiation. Otherwise, the tumor cells could not survive the primary radiation effect and would die.

If the tumor surroundings are so altered (fibrosclerosis) that the nutritive effect of this change cannot be overcome by the adaptability of tumor cells in successive generations, the tumor growth will finally stop and the cell strain will die (clinical cure).

We do not know what adaptive mechanism is at the disposal of the tumor cells other than their ability to form strains of various degrees of differentiation which survive and grow under conditions in which the primary strain would die. (Compare certain forms of metaplasia of normal epithelial tissues.) Most tumors exhibit no microscopic signs of changed differentiation during and after irradiation, nor is it possible to determine microscopically which part of the cytoplasm, nucleus, or cell as a whole has changed during the process of metabolic and radiobiological adaptation. We see only the consequences of this process; namely, the survival, growth, and reproduction in conditions often basically different from those at the site of origin of the tumor itself. (See also Borak.)

It is pointed out in the present communication that concomitant with changed metabolic adaptation of tumor cells to their surroundings, there is an alteration in their radiosensitivity, which, as a rule, is decreased, under different conditions, to various degrees. This changed sensitivity, also called "derived sensitivity" (8), is

thus related to metabolic activity of the tumor cells and to their capacity for adaptation.

More than ten years ago, I called attention to the important interrelations between cyclic changes of the mucous membrane of the larynx and the radiosensitivity of epithelial cancers (26). Not long ago, Ewing (7), after studying the behavior of the regenerated epidermis following irradiation, came to the conclusion that normal epidermis may acquire resistance to the roentgen ray by a process of adaptation and is able to grow under a dosage which originally destroys the pre-existing epidermis. Ewing believed, however, that tumor cells subjected to exactly the same dosage do not exhibit that power of adaptation and regeneration but perish, differing in this respect from normal cells. The cure of cancer seems to depend upon this difference in adaptation, for normal epithelium may regenerate, whereas cancer does not. A consideration of adaptation and regeneration of connective tissue is emphasized as necessary to an understanding of regression of deep parts of the tumor (7, 14).

Our observations show that tumor cells display notable adaptive properties and therefore mostly escape from destruction. They die only if their adaptability cannot overcome the loss of nutritive qualities of the irradiated, adapted, and regenerated connective-tissue stroma.

Recent experimental studies of Failla (8) appear to support this finding. He observed *in vitro* that the nature of the medium in which the tumor cells are found following irradiation (comparable with irradiated stroma) exerts an influence on cell damage. The radiosensitivity manifested by a tumor is the result of an inherent radiosensitivity possessed by its cellular constituents and of a derived radiosensitivity depending for its degree on the characteristics of the medium (stroma, environment of tumors).

The conclusions of Failla, drawn from *in vitro* experiments limited to experimental cancer strains, are thus similar to those of this author based on histologic studies on human tissue. According to Failla, the derived radiosensitivity of tumor cells is induced; consequently, these cells must possess adaptability, without which no changes in sensitivity can be induced. His conclusion that these changes are influenced by the characteristics of the medium are entirely in accord with the results of morphologic examination following irradiation. The latter shows that the medium consists of connective tissue changed by irradiation, or of heterotopic structures.

The above observations and conclusion do not stand in contradiction to older beliefs enumerated in the first part of this article. However, the theory regarding survival of the more resistant of mixed cells present in malignant tumors may well be modified. It may be stated, therefore, that increased resistance of the surviving cells is not intrinsic, but is acquired by irradiation and inherited through successive generations in the presence of the capacity of the tumor cells to adapt themselves to the changed *milieu*. It is of no basic significance in this connection whether the radiobiologic adaptation is directed toward an area of primarily and constitutionally radioresistant tissue invaded by the tumor (cartilage, muscle, fat) or toward a zone which has itself become radioresistant following irradiation (sclerotic connective stroma). The author believes, with Borak, that the native behavior and primary radiosensitivity of the tumor cells are congenital and constitutional and depend to a great extent upon the radiosensitivity of the cells of their origin. The sensitivity of the tumor cell, however, may be modified by adaptation to its changed surroundings. This acquired modification is maintained as long as the modifying conditions remain unchanged.

CONCLUSION

An attempt has been made to analyze the cause of acquired radioresistance of malignant tumors on a cellular basis.

The histologic and radiobiologic behavior of the mucous membrane of the larynx after irradiation may be used as a test experiment for radiobiologic conditions present in the irradiated cancer. Microscopic examination shows that cells of laryngeal epithelium are primarily destroyed by irradiation and that a new and more highly differentiated metaplastic epithelial structure develops after disintegration of the original mucous membrane. This newly developed epithelium possesses lower radiosensitivity. Its cells are characterized by (1) ability to regenerate under doses of irradiation which previously destroyed them; (2) a higher degree of differentiation; (3) a capacity to adapt their metabolism to the nutritive changes of the irradiated, subepithelial connective tissue. Thus the regenerated epithelium displays signs of increased radioresistance.

It is very likely that similar changes take place in the tumor itself. The radiant energy destroys primarily many of the tumor cells; however, a new strain of cells develops from structures which, in the nascent state, were exposed to the direct or indirect effects of irradiation. The new cell generations gradually become more highly differentiated. A change in their radiosensitivity occurs, corresponding to this new degree of differentiation and to the capacity of cellular adaptation to the nutritive properties of the adjacent simultaneously irradiated connective tissue. Tumor cells which are able to adapt themselves maintain their newly acquired properties in successive cell generations. Gradually the entire tumor becomes transformed into a growth, the radiobiological properties of which are adapted to the biological conditions prevailing during and after irradiation. In this new surrounding, the tumor either disintegrates or its radioresistance is increased. The decrease of radiosensitivity of most of the metastatic tumors, of tumors invading muscle, fat, cartilage, bones, etc., finds a natural explanation in their ability to adapt their metabolic and radiobiological properties to those of the new host tissue which is, as a rule, more radioresistant. Anaplastic tumors, which are unable to produce more highly differentiated structures, remain sensitive and disintegrate, due to the direct effect of radiant energy, as long as they grow in their original matrix; however, as soon as they invade heterotopic tissues (displaying their capacity for adaptation), their radiosensitivity decreases. It seems reasonable to assume that "residual" tumors after irradiation, and recurrences of irradiated tumors, must be regarded from a radiobiological standpoint as metastases developing in the bed of the primary tumor, for their growth occurs in a tissue modified to a variable extent by previous irradiation. This modified tumor bed may be considered structurally and radiobiologically as heterotopic tissue, thus explaining the loss of radiosensitivity of "residual" and recurrent tumors.

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EDITORIAL

The Teaching of Radiology

With the post-war resumption of the Annual Conference of Teachers of Clinical Radiology, the problems of undergraduate and postgraduate training in radiology will receive attention that was necessarily diverted to other fields for the period of hostilities. In this connection some reflections presented by James F. Brailsford in the Twenty-Second Mackenzie Davidson Memorial Lecture before the British Institute of Radiology[1] are particularly pertinent. This address presents a challenge to all of us to stop and consider the problems which radiology has surmounted and the course to be charted for the future.

No longer, Brailsford believes, should we welcome to radiology all who show an interest in the subject, regardless of their qualifications. "There are ample reasons," he says, "for believing that the time has now come when we have a right to ask those who wish to use radiology in medical practice to show evidence that they have received a recognized course of training." These ample reasons are to be found in certain "abuses of radiology," which he proceeds to discuss under five headings: (1) neglect of clinical methods by the substitution of more rapid radiological examinations; (2) the time for an x-ray examination; (3) the desire of the spectacular; (4) useless and undesirable radiography; (5) interpretation without knowledge.

In his discussion of the first of these abuses, Brailsford forcibly calls attention to the decline of basic clinical studies in favor of the less time-consuming radiological examination. A diagnosis made solely on x-ray evidence without careful evaluation with the aid of clinical observations may react to the detriment of the patient. Too often symptomless lesions brought to light by radiologic studies have led to surgical exploration which is not only unjustifiable but actually detrimental. Such lesions, when studied over a number of years by able clinicians, with the aid of serial radiographs, have frequently been shown to remain unchanged or relatively so. Brailsford's feeling that the x-ray tube may become discredited if carelessly employed as a time- and thought-saving instrument to the neglect of the more important clinical investigations may well be shared by all thoughtful radiologists.

The second abuse concerns the time at which the examination should be done. In many instances there is a demand for radiographic examination immediately after a serious injury, while the patient is still in shock and before any attention is given to the wound. Not only may this harm the patient, but the radiographic findings are likely to be entirely inadequate in the absence of a preceding physical examination. All of us can recall instances in our own practice when a delay in radiographic examination would have been advantageous. In this connection Brailsford again calls attention to the latent period between the time of the onset of disease and the development of signs recognizable on the roentgenogram, a subject which he has discussed editorially in the columns of this journal (**46:** 184, 1946). Cognizance should also be taken of the fact that improvement of the clinical signs may far outstrip improvement in the radiographic appearance.

The desire for the spectacular, which is designated as the third abuse, is exemplified by the ill-advised use of contrast sub-

[1] Published in Brit. J. Radiol. **18:** 249, August 1945.

stances to visualize structures which are not readily demonstrated on the plain film. This, says Brailsford, should never be done until the patient has a thorough clinical examination and routine radiographs which have been interpreted by a competent observer, for these may provide all the information that is required.

Closely akin to the third abuse is the fourth, namely, useless and undesirable radiography. Under this head are included distressing and painful investigations in cases of hopeless carcinomatosis or other incurable affections, as well as multiple examinations at such brief intervals that no appreciable change in the picture can be expected.

Interpretation without knowledge, the fifth of Brailsford's abuses, is one that concerns every radiologist. Under this heading he describes the many mistakes which may be made—and too often have been made—by those with insufficient knowledge both of clinical medicine and radiology. Adequate training is the rock on which radiology stands, and the determination with which this point is defended by the Board of Radiology will largely determine the respect in which our specialty will continue to be held.

Throughout this lecture Brailsford continually stresses the need of clinical training for those practising radiology, which is as it should be. The radiologist must be able to explain the clinical significance of his findings or he must pass this responsibility on to the clinician. The latter course cannot but jeopardize the position which the radiologist should occupy. This, to be sure, is apparent to those of experience, but too often its deeper significance is overlooked. It means not only that we must ourselves keep abreast of clinical practice, but that those of us upon whom the education of future radiologists depends must insist upon a sound clinical grounding as a basis for training in the specialty we represent.

Malpractice: Honest Difference of Opinion among Physicians as to Proper Method

Under the above title there has recently been published in the J. A. M. A. (132: 350, Oct. 12, 1946) a medicolegal abstract which should be of particular interest to all radiologists—Blakenship *vs.* Baptist Memorial Hospital, 168 S.W. (2d) 491 (Tenn., 1942).

Briefly the facts of the case are as follows. A radiologist was sued because of the occurrence of a third-degree reaction following irradiation of a recurrent Grade IV squamous-cell carcinoma of the uterine cervix. The position taken by the defendant—and in this he was supported by other roentgenologists—was that the treatment administered was of conventional type and the dosage within limits ordinarily accepted as safe. In treating such a cancer, however, he held that the primary consideration was not the effect on the skin but destruction of the tumor, which would otherwise inevitably prove fatal. There had been no further recurrence in his patient following irradiation.

Another radiologist, on the other hand, testifying for the plaintiff, held that "the first consideration is never to damage the skin beyond repair." He attributed the injury to overlapping of the x-rays on the scar tissue incident to the primary operation and stated that the dose administered —2,100 r over a 14-day period—was in the danger zone.

Because of the divergence of opinion among the specialists testifying, the court took the case from the jury on the ground that a jury of laymen was not qualified to determine which method of treatment was right. Since there was no contention that the defendant did not possess the requisite learning and skill, that he made any error in diagnosis, or that he neglected the pa-

tient after the treatment, it was held that, if an excessive dose was given, it was due to an error of judgment and not of negligence.

The Court of Appeals upheld the decision of the original judge in favor of the defendant, ruling that where there is a difference of opinion among physicians or surgeons with reference to the treatment to be given in a particular case, a physician will not be liable for malpractice if he follows the course of treatment advocated by a considerable number of physicians of good standing in his community. The case eventually came to the State Supreme Court, which again upheld the decision in favor of the defendant and handed down the unusual ruling that the case was never one for jury trial, since the arguments and principles involved were such that a jury could not decide.

On reviewing the original testimony in this case, one is impressed by the eminence of the legal talent on both sides, the evidences of careful preparation, and the amount of medical testimony introduced, especially regarding the physics and biological aspects of radiation therapy. Fortunately the ultimate outcome of the action was of benefit to radiology rather than otherwise, since it brought before the public certain aspects of that specialty about which there is much misunderstanding and established a precedent which may be of future usefulness. This, however, does not minimize the serious damage that can be done to roentgenology in general and to a roentgenologist in particular by a fellow roentgenologist testifying in court on points which are primarily matters of judgment.

The abstract appearing in the J. A. M. A. is recommended reading for every radiologist.

ANNOUNCEMENTS AND BOOK REVIEWS

APPLICANTS AND DIPLOMATES AMERICAN BOARD OF RADIOLOGY

There are many Diplomates of the American Board of Radiology, as well as candidates with applications on file, whom it has been impossible to reach at the last known address. During and since the war, many radiologists have changed locations, and these changes do not appear on the records kept in the Secretary's office. It is most important that these records be accurate, and it is therefore urged that every Diplomate whose present address differs from that appearing in the new Third Edition of the "Directory of Medical Specialists" and every applicant with change of address since the filing of his application notify the Secretary immediately.

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ST. LOUIS RADIOLOGICAL SOCIETY

At a recent meeting of the St. Louis Radiological Society, Dr. Wendell G. Scott was re-elected President, and Dr. Edwin C. Ernst Secretary.

PENNSYLVANIA RADIOLOGICAL SOCIETY

The Thirty-second Annual Meeting of the Pennsylvania Radiological Society will be held on Friday and Saturday, May 9 and 10, at Pocono Manor Inn, Pocono Manor, Penna. Dr. Samuel G. Henderson, Chairman of the Program Committee, has announced the following speakers: Ralph D. Bacon, M.D., of Erie, Penna., Aubrey O. Hampton, M.D., of Washington, D. C., C. L. Hinkel, M.D., of Danville, Penna., Reuben Alley, M.D., of Pittsburgh, Paul C. Swenson, M.D., and Francis F. Hart, M.D., of Philadelphia, S. Gordon Castigliano, M.D., of Philadelphia, Lowell L. Erf, M.D., of Philadelphia, Robert F. McNattin, M.D., of Harrisburg, and Ross Golden, M.D., of New York City. The banquet will be held Saturday at 7:00 P.M., and at that time the scientific exhibit awards will be presented.

Hotel reservations should be secured at once from Pocono Manor Inn.

THIRD AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY

The Third American Congress on Obstetrics and Gynecology will be held Sept. 8–12, in St. Louis. In addition to the general sessions for all groups making up the Congress, there will be smaller group meetings and round-table discussions on pertinent subjects, as well as concurrent sessions for nurses, hospital administrators, and public health workers. Further information may be obtained from the office of the Congress, 24 West Ohio St., Chicago 10, Ill.

DR. ROBERT KIENBÖCK

It has recently been learned on good authority that Dr. Robert Kienböck, well known to many American radiologists, is still living in Vienna, having, however, suffered a stroke. If any of his colleagues here would like to remember him with parcels of food or a friendly letter, he may be reached at the following address: Dr. med. Robert Kienböck, Klumpfelberggasse 3, Vienna 17, Austria.

BOOKS AND WORLD RECOVERY

The continued need for American publications to serve as tools of physical and intellectual reconstruction abroad has been made vividly apparent by appeals from scholars in many lands. The American Book Center for War Devastated Libraries has been urged to continue meeting this need at least through 1947. The Book Center is therefore making a renewed appeal for American books and periodicals—for technical and scholarly books and periodicals in all fields and particularly for publications of the past ten years. They will especially welcome complete or incomplete files of RADIOLOGY.

Contributions should be shipped to the American Book Center, c/o The Library of Congress, Washington 25, D. C., freight prepaid. Further information may be had by addressing the Center.

In Memoriam

DONALD CAMERON GORDON, M.D.

Donald Cameron Gordon of Scranton, Penna., died following a cerebral hemorrhage on Jan. 9, 1947, the fifty-second anniversary of his birth. Dr. Gordon, prominent x-ray specialist and immediate past president of the Lackawanna County (Penna.) Medical Society, was a native of Ottawa, Canada. He fought in France with the famed "Princess Pat" regiment of the Canadian Army in World War I and entered medical school at the close of the war, receiving his degree from McGill University Faculty of Medicine in 1922. He practised in Carbondale for twelve years and was roentgenologist at the Carbondale General Hospital before going to Scranton in 1936 as an associate of the late Dr. Byron H. Jackson, one-time president of the Radiological Society of North America. Dr. Gordon took over Dr. Jackson's practice upon the latter's death in 1939. In August 1942, he enlisted for active duty in the Army and returned from that service in November 1945, with the rank of lieutenant colonel. He served as chief of radiology at Camp Pickett, Va., Woodrow Wilson Hospital, Staunton, Va., and at Fort Leonard Wood, Mo. He was a diplomate of the American Board of Radiology; a member of the Radiological

Society of North America, the Pennsylvania Roentgenological Society, the American College of Radiology, the Philadelphia Roentgen Ray Society and the Central New York State X-ray Society. He is survived by his widow and a brother.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

RADIOLOGY FOR MEDICAL STUDENTS. By FRED JENNER HODGES, M.D., Professor and Chairman, Department of Roentgenology, University of Michigan; ISADORE LAMPE, M.D., Associate Professor, Department of Roentgenology, University of Michigan, and JOHN FLOYD HOLT, M.D., Assistant Professor, Department of Roentgenology, University of Michigan. A volume of 424 pages, with 103 plates. Published by The Year Book Publishers, Inc., 304 S. Dearborn St., Chicago 4, Ill. Price $6.75.

RADICAL SURGERY IN ADVANCED ABDOMINAL CANCER. By ALEXANDER BRUNSCHWIG, M.D., Professor of Surgery, University of Chicago. A volume of 324 pages, with 116 illustrations and 16 tables. Published by the University of Chicago Press, Chicago, 1947. Price $7.50.

X-RAY DIFFRACTION STUDIES IN BIOLOGY AND MEDICINE. By MONA SPIEGEL-ADOLF, M.D., Professor of Colloid Chemistry and Head of the Department of Colloid Chemistry, Temple University School of Medicine, and GEORGE C. HENNY, M.S., M.D., Professor of Medical Physics and Head of the Department of Physics, Temple University School of Medicine. A volume of 215 pages, with 86 illustrations. Published by Grune & Stratton, Inc., New York, 1947. Price $5.50.

ACTIONS OF RADIATIONS ON LIVING CELLS. By D. E. LEA, M.A., Ph.D., Prophit Student of the Royal College of Surgeons, Formerly Fellow of Trinity College, Cambridge. A volume of 402 pages, with 83 tables, 4 plates, and 61 figures. Published by Macmillan Company, New York, 1947. Price $4.50.

Book Reviews

THE LUNG. By WILLIAM SNOW MILLER, Late Emeritus Professor of Anatomy, University of Wisconsin. A volume of 222 pages, with 168 illustrations in black and white and in color. Published by Charles C Thomas, Springfield, Ill. 2nd edition, 1947. Price $7.50.

The second edition of this popular monograph on the anatomy of the lung presents the subject in an authoritative and comprehensive manner. To the superb illustrations of the earlier edition, 3 new color plates and 16 figures in black and white have been added. In no other work is the detailed anatomy of the lung presented so attractively and so clearly.

As is pointed out in the preface, no fundamental change has been made from the first edition. The division into twelve chapters, devoted for the most part to structural elements of the lung, is retained. Chapter 11 is an interesting historical sketch, presenting the conceptions of the earlier anatomists on the structure of the lung and tracing the development of our knowledge from the 17th century to the present day. A full bibliography is appended.

This monograph is a classic which deserves a place in the library of every physician and medical institution. Happily the publisher has matched the excellence of the text with a format of more than usual attractiveness.

X-RAYS AND RADIUM IN THE TREATMENT OF DISEASES OF THE SKIN. By GEORGE M. MACKEE, M.D., Professor of Clinical Dermatology and Director, Department of Dermatology (Skin and Cancer Unit), New York Post-Graduate Medical School and Hospital, Columbia University, and ANTHONY C. CIPOLLARO, M.D., Assistant Professor of Dermatology and Assistant Director of Department of Dermatology (Skin and Cancer Unit), New York Post-Graduate Medical School and Hospital, Columbia University. Contributor, HAMILTON MONTGOMERY, M.D., Associate Professor of Dermatology, Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota, Rochester, Minn. A volume of 668 pages, with 321 engravings and 4 colored plates. Published by Lea & Febiger, Philadelphia, 4th edition, thoroughly revised, 1946. Price $10.00.

It has been eight years since the last edition of MacKee and Cipollaro's standard text on "X-Rays and Radium in Treatment of Diseases of the Skin" appeared. As might be expected, there is no outstanding change in the work, as there have been no marked changes in radiation therapy as it applies to dermatology in the interval. Perhaps the chief addition to the dermatologist's armamentarium has been chemotherapy and the authors call attention to the superior results obtained with the sulfonamides and penicillin in certain skin conditions.

The sequence of subjects is the same as in the third edition, except that Quimby's chapter on Spectroscopy has been omitted. The chapter on The Time-Intensity Factor and Tissue Recuperation has probably undergone the greatest revamping, being much briefer than formerly. The treatment of the physics of x-rays and radium, and of the action of radiation on the tissues, is particularly satisfactory.

To those who are familiar with this authoritative text, it needs little further in the way of recommendation. It continues to merit the favorable recognition it has long received, as an outstanding work in an important field.

RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES

Editor's Note: Secretaries of state and local radiological societies are requested to cooperate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates. Address: Howard P. Doub, M.D., The Henry Ford Hospital, Detroit 2, Mich.

UNITED STATES

RADIOLOGICAL SOCIETY OF NORTH AMERICA. *Secretary-Treasurer*, Donald S. Childs, M.D., 607 Medical Arts Bldg., Syracuse 2, N. Y.

AMERICAN RADIUM SOCIETY. *Secretary*, Hugh F. Hare, M.D., 605 Commonwealth Ave., Boston 15, Mass.

AMERICAN ROENTGEN RAY SOCIETY. *Secretary*, Harold Dabney Kerr, M.D., Iowa City, Iowa.

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LOS ANGELES COUNTY MEDICAL ASSOCIATION, RADIOLOGICAL SECTION. *Secretary*, Moris Horwitz, M.D., 2009 Wilshire Blvd., Los Angeles 5. Meets second Wednesday of each month at County Society Bldg.

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DENVER RADIOLOGICAL CLUB. *Secretary*, Washington C. Huyler, M.D., Mercy Hospital, 1619 Milwaukee, Denver 6. Meets third Friday of each month, at the Colorado School of Medicine and Hospitals.

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SHREVEPORT RADIOLOGICAL CLUB. *Secretary*, Oscar O. Jones, M.D., 2622 Greenwood Road. Meets monthly September to May, third Wednesday, 7:30 P.M.

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NEBRASKA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, O. A. Neely, M.D., 924 Sharp Building, Lincoln. Meetings third Wednesday of each month at 6 P.M. in either Omaha or Lincoln.

New England

NEW ENGLAND ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, George Levene M.D., Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday at Boston Medical Library.

New Hampshire

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RADIOLOGICAL SOCIETY OF NEW JERSEY. *Secretary*, W. H. Seward, M.D., Orange Memorial Hospital, Orange. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called.

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OHIO RADIOLOGICAL SOCIETY. *Secretary*, Henry Snow, M.D., 1061 Reibold Bldg., Dayton 2. Next meeting at annual meeting of the Ohio State Medical Association.

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RADIOLOGICAL SOCIETY OF THE ACADEMY OF MEDICINE (Cincinnati Roentgenologists). *Secretary-Treasurer*, Samuel Brown, M.D., 707 Race St., Cincinnati 2. Meets third Tuesday of each month.

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Wisconsin

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UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE. Meets first and third Thursdays 4 to 5 P.M., September to May, inclusive, Room 301, Service Memorial Institute, 426 N. Charter St., Madison 6.

CANADA

CANADIAN ASSOCIATION OF RADIOLOGISTS. *Honorary Secretary-Treasurer*, E. M. Crawford, M.D., 2100 Marlowe Ave., Montreal 28, Quebec. Meetings in January and June.

LA SOCIÉTÉ CANADIENNE-FRANCAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES. *General Secretary*, Origéne Dufresne, M.D., Institut du Radium, Montreal. Meets on third Saturday of each month.

CUBA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA. Offices in Hospital Mercedes, Havana. Meets monthly.

MEXICO

SOCIEDAD MEXICANA DE RADIOLOGÍA Y FISIOTERAPIA. *General Secretary*, Dr. Dionisio Pérez Cosío, Marsella 11, México, D. F. Meetings first Monday of each month.

ABSTRACTS OF CURRENT LITERATURE

ROENTGEN DIAGNOSIS

RADIOTHERAPY

EFFECTS OF RADIATION

ROENTGEN DIAGNOSIS

THE HEAD AND NECK

A Method of Encephalography. E. Graeme Robertson. Surgery 19: 810–824, June 1946.

A method is described whereby, through posturing the neck, gas can be delivered with certainty from the lumbar puncture site into any portion of the cerebral subarachnoid space, or into the ventricles of the brain. By the use of this method an accurate analysis of the influence of posture on the distribution of air within the cerebrum has been made. The progression of gas through the subarachnoid and ventricular spaces depends solely on the physical laws of hydrodynamics, and is independent of vascular pulsation, since the same effects are obtained in the cadaver. The paths that will be taken by gas injected in the lumbar region are given for all possible positions, including (1) supine, with head extended and flexed, (2) prone, with head extended and flexed, and (3) upright, with head extended and flexed to varying degrees. A clear analysis is made of the reasons why the various routes are taken, and the proper views to be made at each stage of filling are indicated.

Briefly, the technic is as follows: After suitable preparation, the patient is supported upright before apparatus that enables postero-anterior and lateral skull films to be made without moving the head. Two lumbar puncture needles are inserted in adjacent lumbar interspaces. Oxygen is introduced through the upper needle, while fluid is allowed to escape through the lower. Constant normal pressure is maintained, as indicated by a manometer attached to the lower needle.

From full flexion the head is gradually extended until the cisterna magna, fourth ventricle, aqueduct, third, and lateral ventricles are filled in turn. Posturing for filling other portions of the cerebrospinal fluid spaces is described. Films are made in successive stages of filling, and the position of the head is changed so as to direct the filling of whatever cavities it is desired to visualize. When the ventricles are satisfactorily filled, the patient is placed in the recumbent position and the following views are made: anteroposterior, postero-anterior, and both stereoscopic laterals. Additional views which may be taken, according to the region suspected of harboring pathological processes, are the lateral with the face up and anteroposterior with the head in lateral decubitus. These films are then studied before the patient is returned to his room, and special views are made as indicated.

The entire procedure requires about sixty minutes. In 500 examinations by this method, including over sixty neoplasms, no serious complications were observed. Some of the neoplasms were in the cerebral hemispheres, some were suprasellar, and some were in the posterior fossa. However, when there is much elevation of the lumbar cerebrospinal fluid pressure, or with indications of incisural or foraminal herniation, ventriculography is done.

Causes of failures are discussed, with corrective maneuvers for each. A detailed discussion of posturing to investigate the posterior fossa, with excellent diagrams, is presented. For a thorough description of the entire procedure of insufflation of air into the cerebrospinal fluid spaces through lumbar injection, with the patient upright, the reader is referred to the original article.

JOHN E. WHITELEATHER, M.D.

The Use of Laminagraphy with Encephalography in the Diagnosis of Midline and Subtentorial Brain Tumors. Bernard S. Epstein and Leo M. Davidoff. Am. J. Roentgenol. 55: 675–688, June 1946.

Visualization of the 3d and 4th ventricles, the aqueduct of Sylvius, the basilar cisterns, and the cerebellum is particularly important in the diagnosis of midline and subtentorial brain tumors. These structures are frequently difficult to demonstrate by pneumoencephalography, and particularly by ventriculography. They are often obscured by the paranasal sinuses, the mastoid cells, petrous pyramids, and air in the convolutional sulci. Much more frequent visualization of the midline structures may be obtained by adding body-section roentgenography to the routine pneumoencephalographic procedures.

With the authors' technic, the standard pneumoencephalographic exposures are made and the wet films are examined. Following this the patient is transferred to the laminagraphic room and placed in the prone position, the head being positioned as for a lateral roentgenogram. A lateral laminagram is made through the sagittal plane in the midline and either 0.5 or 1 cm. above the midline, with the head in right and left lateral positions. Other views are obtained as required for the individual patient. Results with laminagraphy in the postero-anterior and anteroposterior positions have not warranted their routine use.

The roentgenographic anatomy of the midline structures is reviewed.

The authors have made laminagrams as a part of the pneumoencephalographic examination in approximately 100 patients. Fifteen of these had tumors encroaching on midline structures. Review of these cases in addition to 30 control cases which did not have subtentorial or midline tumors showed visualization of the midline structures by the laminagrams to be consistently better than in the routine pneumoencephalograms. Six case reports illustrating the authors' observations are included.

H. H. WRIGHT, M.D.

Subdural Pneumography. Campbell Howard. Am. J. Roentgenol. 55: 710–716, June 1946.

The author describes a technic for subdural pneumography and discusses the anatomical features which are revealed by this procedure. By this method the normal and abnormal attachments between the cerebral cortex and dura, not visualized with the usual subarachnoid air injection, are demonstrable.

The method of introduction of air into the subdural space is described. The roentgenograms are made at a 6-foot tube-film distance with the use of a small cone without a grid. Five anteroposterior and three lateral roentgenograms are made, with the head in varying degrees of flexion and extension. A second series of films is taken twenty-four hours later. The procedure is less distressing to the patient than encephalography, but headache and nausea may be produced. The patient is prepared with 9 to 12 gr. of phenobarbital in divided doses, beginning four hours before the operation, the last dose being given one hour before it. Sudden changes in the position of the head may cause considerable distress. The discomfort described by the patients closely resembles the headache, nausea, and vomiting attending migraine.

Normally the subdural space is a potential one only, with no communication between it and the subarachnoid space. After the subdural introduction of air the cortex falls away from the dura over the vault, leaving a space of variable depth. There are no normal attachments between the arachnoid and the dura in this region except adjacent to the sagittal sinus. There is a wide variation in size and extent of these attachments. Arachnoidal granulations may extend into the dura, producing erosions of the inner table of the skull and fixing the cortex to the skull and dura. The corticodural attachment may be considerably widened in the presence of large arachnoidal granulations.

When air enters the subdural space during encephalographic examination, it probably indicates a tear in the arachnoid or an arachnoidal fistula. In some instances there is greater separation of cerebral cortex and cranial vault on one side than on the other. In these instances, if the ventricles are air-filled, downward displacement of the ventricle is demonstrated on the side of greatest corticodural separation. This is not noted without air in the subdural space. In subdural pneumography this corticodural separation occurs with air at atmospheric pressure. These findings suggest that the subdural space maintains a negative pressure and that it is this negative pressure rather than the corticodural attachment which determines the normal relationship between the cortex and the cranial vault.

H. H. WRIGHT, M.D.

Discussion on Cortical Atrophy. Harvey Jackson and John J. Fleminger. Proc. Roy. Soc. Med. **39:** 423–430, May 1946.

Jackson discusses the etiology of cortical atrophy, mentioning as possible causes trauma (including that incident to repeated convulsive therapy), injury due to intensive x-ray therapy for cerebral tumors, and infections and vascular disturbances producing localized areas of encephalitis. He states that the differentiation between tumor and atrophy may be reached clinically, but as a basis of treatment confirmatory evidence should be obtained by encephalography or ventriculography. Gross defects in the radiographic appearances are easy enough to interpret, but just how much alteration in a film is essential to confirm the presence of atrophy is uncertain. It is Jackson's impression that accumulations of air over the parietal cortex are evidence of abnormality, especially if these are demonstrated with the patient in the "horizontal posture." The relative size of the ventricular system and the skull are considered, and Evans (Arch. Neurol. & Psychiat. **47:** 931, 1942. Abst. in Radiology **40:** 206, 1943) is quoted on this point. Judging from his figures, the normal ratio between the transverse diameter of the anterior horns and internal diameter of the skull is not less than 1:3.

From 71 cases of cortical atrophy, Fleminger selected for study 12 cases, presenting clinically as cerebral tumors and probably allied in pathology to the presenile dementias, but differing from these in the absence of dementia. Clinical features included epilepsy of all varieties, with transient attacks of paresis of the limbs, dysphasia, headaches, and attacks of dizziness.

Plain films showed no significant abnormality. The characteristic features discovered on encephalography or ventriculography were dilatation of the ventricles either bilaterally or unilaterally, without any shift in the ventricular system, and, more striking, an increase in the convolutional markings in the subarachnoid space, revealing widened sulci. Subdural puddles of air at the frontal and occipital poles and down the side of the falx were frequently seen and were sometimes demonstrable in the temporal region, in ventriculograms. In this connection mention is made of the increase in depth of the subdural space and the lax, sometimes wrinkled dura found when the burr hole for ventriculography has been made. These were often the first indications that one was not dealing with a space-occupying lesion. "One important fact is that, although the physical signs and the symptoms may point to only a local cortical lesion, and in fact there may only be a unilateral ventricular dilatation, this is not always the case, and frequently the area of atrophy as demonstrated by air studies is seen to extend over a wide distribution and often to the opposite hemisphere."

When the roentgen findings were not characteristic, operation was helpful in making a diagnosis, and pathological examination of tissues removed left no doubt as to the condition, though it gave no accurate classification of the nature of the changes.

[A detailed analysis of the roentgen diagnosis of cortical atrophy is not given in this article, but from the reproductions, it is obvious that the amount of air in the subarachnoid space is greater than the 1 to 3 mm. considered normal (see, The Head and Neck in Roentgen Diagnosis, by Pancoast *et al.*, p. 744).]

SYDNEY F. THOMAS, M.D.

Coarctation of the Walls of the Lateral Angles of the Lateral Cerebral Ventricles. Leo M. Davidoff. J. Neurosurg. **3:** 250–256, May 1946.

Asymmetry of the two lateral ventricles of the brain, observed in certain clinical cases in which pneumoencephalography was done for various reasons, such as epilepsy or post-traumatic headache, was investigated. This asymmetry consists of a normal looking "butterfly-wing" pattern of the ventricle on one side and a truncated one on the other. Since the normal appearing ventricle was also of normal size, the asymmetry obviously could not be explained on the basis of a unilateral dilatation, and the obvious conclusion had to be reached that the smaller ventricle was the anomalous one. The possible causes for this appearance were believed to be: (1) inadequate filling of the ventricle with gas; (2) a filling defect produced by a tumor; (3) adhesions resulting from a healed inflammatory process; (4) a congenital anomaly. The first two possibilities were ruled out by clinical and roentgenologic studies and the third appeared highly improbable in view of the case histories. That the fourth explanation was the correct one was shown in a study of 64 brains taken routinely from patients dying from causes chiefly other than neurological. Among the 64 specimens, 6 showed asymmetry of the ventricles on postmortem ventriculograms; 10, deviation of a similar nature on coronal section; 4, positive roentgenographic changes and corresponding pathological changes. The asymmetry was found to correspond to an area of coarctation of the ventricular walls usually at or near the extreme lateral angle of one ventricle. This is believed to take place during the developmental period of the brain.

Reversibility of Cerebral Ventricular Dilatation. Henry A. Shenkin and Charles R. Perryman. J. Neurosurg. **3:** 234–238, May 1946.

Three cases of internal hydrocephalus caused by an obstructing lesion in either the third or fourth ventricle

were studied by ventriculography before and ventriculoencephalography after relief of the obstruction. In each patient, the lateral ventricles were smaller after operation, showing, in the authors' opinion, that ventricular size in many instances is reversible if the dilatation of the ventricles is due to an obstructive lesion and the obstruction has not been present too long. Roentgenograms are reproduced.

Extensive Erosion of the Base of the Skull from a Leptomeningeal Cyst. Report of a Case. Arthur B. Soule, Jr., and Benjamin B. Whitcomb. Arch. Neurol. & Psychiat. **55:** 382–387, April 1946.

Leptomeningeal cysts are collections of clear or xanthochromic fluid located within the subarachnoid or subdural space or between the layers of dura. They usually occur following severe trauma to the skull with damage to the leptomeninges. Clinical evidence of these cystic lesions may not be manifest for months or years after injury. The usual roentgenologic findings consist of thinning and bulging of bone immediately adjacent to the lesion. Rarely there is complete erosion of both tables, with bulging of the cyst into pericranial soft tissues. In either event, the changes are most often seen in the parietal, frontal, and occipital regions.

Soule and Whitcomb report the case of a 28-year-old soldier in whom a leptomeningeal cyst was discovered one and one-half years following a mild cerebral concussion resulting from a bomb explosion. The outstanding feature of the case was the unusual location in the floor of the middle cranial fossa. Erosion of bone, best seen in the verticosubmental view and in the oblique projections of the orbits, was so extensive that the entire cyst appeared to be completely outside the cranial cavity. The differential diagnosis and successful surgical treatment of the lesion are described.

JOHN F. HOLT, M.D.
(University of Michigan)

Some Observations on the Morphologic Evolution of the Osseous Changes in Paget's Disease with Particular Reference to Changes in the Skull of the Type of So-Called "Osteoporosis circumscripta." Mario Paoletti. Arch. di radiol. (Naples) **18:** 237–248, November-December 1942.

The author presents roentgenograms (in 12 full-page plates) of two cases of Paget's disease which he followed for four to six years. Both patients presented the typical changes of osteoporosis circumscripta of Schüller in the skull and both had other lesions typical of Paget's disease in several bones. E. T. LEDDY, M.D.

Linear Fracture of the Skull Across the Venous Sinuses. Arthur D. Ecker. New York State J. Med. **46:** 1120–1121, May 15, 1946.

Linear fractures or diastatic injuries to sutures of the skull may cross the major venous sinuses and produce obstruction of venous outflow even though there is no bone depression. The impaired venous outflow may, in turn, produce headache, mental confusion, and papilledema. Comparative Queckenstedt tests on both sides demonstrate the venous impairment. Queckenstedt tests are not conclusive but when considered in connection with the clinical course and the location of the injury are very helpful. Prompt recognition of the condition and conservative management, with maintenance of upright posture, may prevent unnecessary surgical exploration and ventriculography. The latter procedure is difficult, since the ventricles tend to be small and the injected air is often forced out of them into the subarachnoid space.

Two cases are briefly reported. In each instance the patient was kept up and about, and in each there were fairly prompt subsidence of papilledeam and full recovery. ROBERT C. PENDERGRASS, M.D.

Neurofibromatosis with Defect in Wall of Orbit. Report of Five Cases. William T. Peyton and Donald R. Simmons. Arch. Neurol. & Psychiat. **55:** 248–265, March 1946.

Neurofibromatosis is a congenital defect of hereditary nature which was originally described by von Recklinghausen as being characterized by cutaneous tumors and pigmentation (*café au lait* spots). It has since been shown that the disease may manifest itself in many other ways, and of the changes which have been described, those involving the osseous system are perhaps the most remarkable. The long list of osseous abnormalities in this condition includes such defects as scoliosis, kyphosis, overgrowth and undergrowth of individual bones, central and peripheral cyst-like defects, and pseudarthroses. In the skull one may find bulging of circumscribed areas, peculiar vascular designs, temporal or parietal bossing, localized erosion and atrophy of the vault, various types of gross asymmetry, and other defects.

To the relatively large group of patients with skull lesions reported as occurring in conjunction with neurofibromatosis, Peyton and Simmons add 5 more, each with a defect in the wall of an orbit permitting free communication between that structure and the intracranial cavity. Although pulsating exophthalmos was present in all 5 cases, in at least 2 instances a retrobulbar neurofibroma was not present, the orbital defect existing as a related but separate anomaly. In such circumstances, the exophthalmos obviously was due to encroachment on the orbit by the brain and meninges.

Roentgenographic examination will serve to identify the defect in the orbit, but it may be overlooked if films are not carefully scrutinized. Orbital enlargement with increase in density of that structure, absence of the normal markings in the orbital roof, and deformities of the sella turcica are some of the abnormalities which may be observed. The roentgenologist should always consider the possibility of neurofibromatosis as an etiological factor when orbital defects are encountered.

JOHN F. HOLT, M.D.
(University of Michigan)

Ethmoido-Sphenoidal Hypertrophy with Endocranial Protrusion. Dino Agati. Radiol. med. (Milan) **32:** 151–154, May 1946.

Agati reports two cases of marked hypertrophy of the sphenoid sinus. Both patients were adults, with visual symptoms beginning about a year before medical help was sought. Ophthalmic examination revealed bilateral temporal hemianopsia and the patients were suspected of having sellar tumors. For this reason they were sent to the radiologist, who found normal sellar contours with marked protrusion of the anterior portion of the roof of the sphenoid sinus into the cranial cavity. Agati believes that this protrusion caused enough impingement on the optic nerves to explain the visual syndrome.

CESARE GIANTURCO, M.D.

THE CHEST

Roentgenographic Scanning of the Chest. Sherman W. Atwell. Dis. of Chest **12:** 222–227, May-June 1946.

Because the conventional chest film may be inaccurate and misleading and a simple stereoroentgenogram is not always entirely comprehensive, the author has devised a method whereby two stereoroentgenographic examinations are made of a given part, in two positions, on one set of films. This is accomplished by the use of lead strips to block half the film either vertically or horizontally, depending upon whether one wishes to study the right or left or the upper or lower half of the thorax. In especially intricate areas, such as the subthoracoplasty lung, information can frequently be gained by using both blocks and taking four "scanning" views. With this method, one avoids the necessity of changing films for a comparison study, with the lag in memory which makes such comparison so uncertain.

HENRY K. TAYLOR, M.D.

The Middle Lobe of the Left Lung. Aldo Piergrossi. Radiol. med. (Milan) **32:** 154–165, May 1946.

Piergrossi describes the radiological appearance of the middle lobe of the left lung. This lobe corresponds very closely to the right middle lobe in its anatomical and radiological characteristics. Its recognition is important because of the surgical implications.

CESARE GIANTURCO, M.D.

The Normal Lung Markings and Their Variations with Age. Giovanni Gardella. Radiol. med. (Milan) **32:** 173–192, June 1946.

Gardella states that the most important changes in the pulmonary markings occur in infancy and in old age. These changes consist of a progressive increase of aerated tissue separating vessels and bronchi. During infancy and adult life this aerated tissue is normal pulmonary tissue. In old age a gradual destruction of the alveolar septa leads to a varying degree of emphysema.

CESARE GIANTURCO, M.D.

On Retrocardiac Pulmo-Pleural Demarcation Lines and Their Diagnostic Significance. L. Billing. Acta radiol. **27:** 257–263, May 6, 1946. (In English.)

The importance of studying the pneumo-pleural lines on chest roentgenograms in order to detect slight densities which may indicate pathologic pulmonary or pleural processes has been stressed by Edling (Acta radiol. **23:** 595, 1942. Abst. in Radiology **45:** 200, 1945). A pleural process as a rule displaces or deletes a considerable portion of the lung contour. In the present paper the author confines his discussion to local breaks in contour, which have proved an indirect sign of parenchymatous induration. This sign is particularly valuable in diagnosing retrocardiac processes, as a defect in the aortic contour is fairly often the only unequivocal evidence of some slight lung process which cannot be projected free, whatever the direction of the x-ray beam. Such defects are not always of pathologic significance, however, as they may be due to some anatomical variation in the posterior mediastinum. The author gives the physical and anatomic basis for these observations.

To study details of retrocardiac parts of the lungs, roentgenograms should be taken with considerably heavier exposure than the usual frontal views (sagittal radiation) and with the use of a grid. Three demarcation lines have been found useful: the border line between the diaphragm and the lung in the postero-anterior and lateral views, the retrocardiac lines in the frontal view, and the borderline between the wall of the thorax and the lung in the lateral view. Only the retrocardiac pulmo-pleural lines on the left side are discussed here.

Silicosis, the Most Important of the Pneumoconioses. Norbert Enzer. Occupational Med. **1:** 425–442, May 1946.

The term "pneumoconiosis" embraces all forms of pulmonary reactions to the inhalation of inorganic dusts. Silicosis is the most important of these but is rarely pure or uncomplicated, for there is often an adulterating dust affecting the character of the lesions in various ways and degrees. The rate at which the disorder will develop depends on the intensity of dosage, and this involves consideration not only of the total amount of dust inhaled but of the length of time over which it is inhaled and its chemical and physical structure. The more finely divided the silica, the more serious its effect.

The essential anatomic features of the silicotic lung may be summarized as follows: (1) a nodular fibrosis scattered throughout both lungs, associated with a similar formation in the corresponding lymph nodes; (2) coal or dust pigment in the areas of fibrosis in the lungs, lymph nodes, and pleura; (3) pigmentation and some fibrous thickening of the pleura; (4) microscopic emphysema in the region of the nodule only, widely disseminated and uniform emphysema, and irregular or bullous emphysema; (5) increased number of nodules, with a tendency to conglomeration; (6) progressive enlargement and induration of the hilar lymph nodes, often to the point of massive fixation; (7) evidence of bronchitis and bronchiolitis; (8) strain on the right side of the heart, indicated by hypertrophy of the right ventricle and dilatation of the right chambers; (9) tuberculosis in any of its forms.

With an understanding of the anatomic pattern of silicosis, one may more accurately interpret the roentgenologic manifestations. In most cases the simple roentgenogram is adequate for diagnosis. But for the detection of emphysema, mediastinal nodes, and effects on the heart, highly technical and refined methods of examination are necessary, calling for the most highly skilled and trained radiologists. Planigraphy and angiocardiography have not been used up to now as often as would be desirable; thus many of the effects of silicosis are not detected, and understanding and explanation of the symptoms are not achieved. When these special procedures are applied in more cases, there will be a closer approximation of the clinical behavior, physiologic disturbance, and pathologic conditions.

Coexistent Pulmonary Asbestosis and Sarcoidosis. John H. Skavlem and Robert J. Ritterhoff. Am. J. Path. **22:** 493–517, May 1946.

Sarcoidosis and pulmonary asbestosis present many clinical and roentgenographic similarities and are alike also in their more frequent fatal complications, namely, pulmonary tuberculosis and cardiopulmonary insufficiency. A unique case of coexisting asbestosis and sarcoidosis is reported, the only example of either condition in a series of 1,870 necropsies at Dunham Hospital (Cincinnati).

The patient, a 42-year-old male, had worked in an

asbestos plant for twenty-five years. Previous to December 1943 he noticed that slight activity produced shortness of breath, though he was able to lie flat in bed without respiratory difficulty. There was no history of cough, hemoptysis, or cardiac embarrassment. The patient lost 22 pounds in weight from December 1943 to March 1944, at which time he presented himself for medical care. The anteroposterior diameter of the chest was increased. Respiratory excursions were equal but decreased. The percussion note was resonant, and auscultation revealed fine râles over the bases of the lungs posteriorly. There was no evidence of cardiac enlargement, irregularity, or decompensation. A roentgenogram of the chest revealed moderate enlargement of the hilar shadows bilaterally. One calcified area was present in each hilum, with numerous small nodular densities scattered through both lung fields, especially throughout the lower lobes. There was some confluence of the densities in the left lower lobe. Emphysema was present. The sedimentation rate was 26 mm. Vital capacity was 51 per cent of normal. Tuberculin tests were not done.

The patient was seen at regular intervals, and his only complaint was increasingly severe exertional dyspnea. A roentgenogram of the chest four months after the original film revealed nothing further. Dyspnea became progressively more severe, so that eventually, even at bed rest, there was extreme air hunger. At no time was there evidence of cardiac failure. Death occurred approximately eleven months after the onset of symptoms, apparently from respiratory failure. The primary findings at autopsy were a moderate pulmonary asbestosis and extensive sarcoidosis of pulmonary and tracheobronchial lymph nodes.

Clinically, in view of the significant history of exposure to asbestos, the possibility of sarcoidosis was never entertained. In retrospect, the rapidly progressive disabling dyspnea, unaccompanied by evidence of enlargement of the right heart or cardiac failure, should have aroused suspicion that there was a concomitant pulmonary lesion. Asbestosis alone is not usually accompanied by such profound, rapidly developing, respiratory embarrassment. It would seem that a clinical diagnosis of coexistent asbestosis and sarcoidosis would be justified only by biopsy of a lymph node or a skin lesion to demonstrate sarcoid lesions and the discovery of asbestos fibers in the sputum, with a history of adequate exposure to asbestos and roentgen evidence of diffuse pulmonary fibrosis.

Latent Silicosis and Tuberculosis. Howard Dayman. Am. Rev. Tuberc. **53:** 554–559, June 1946.

Clinical and experimental studies have shown that silicosis renders the patient more susceptible to tuberculosis, but the degree of silicosis required to bring about this alteration in resistance is not clearly defined. Four case reports are presented to show that silicosis of such a degree as not to be clearly demonstrable on roentgenograms of good technical quality may exert a harmful effect on the resistance to tuberculosis. In none of the patients was typical silicotic nodulation present at first. In three, the periods of exposure to silica dust were relatively short—seven, fourteen, and five years respectively. The development of nodulation late in the course of the disease appeared to be due to the fact that tuberculosis accelerates the growth and enhances the size of the silicotic nodule. The development of tuberculous disease about the nodule also contributes to a more conspicuous shadow on the roentgenogram. L. W. PAUL, M.D.

Importance of Systematic Radiophotography in Case Finding of Pulmonary Tuberculosis. O. M. Mistal. Schweiz. med. Wchnschr. **76:** 405–410, May 11, 1946.

The author reports the results of a photofluorographic survey in Switzerland covering 10,026 cases. He divides his material into two groups, 4,840 adults and 5,186 children. In the first group there were 3,820 normal chests, 719 minor changes in morphology, 267 cases of controllable disease, of which 67 were pulmonary tuberculosis, 34 cases of serious disease, of which 25 were pulmonary tuberculosis. In the second group, 4,634 were normal, 215 showed minor alterations, 332 showed controllable disease (118 cases of pulmonary tuberculosis), and 5 showed serious disease (2 cases of pulmonary tuberculosis). The relatively small percentage of serious tuberculosis in the younger group is believed to be due to the careful examination of school children which is generally practised in Switzerland. The author feels that the use of photofluorography is an important adjunct to the control of tuberculosis, particularly in those countries which have undergone the hardships of war. LEWIS G. JACOBS, M.D.

A Mass Chest X-Ray Survey in Philadelphia War Industries. William F. Elkin, Mary A. Irwin, and Charles Kurtzhalz. Am. Rev. Tuberc. **53:** 560–565, June 1946.

The present report details the results of a mass chest x-ray survey of 71,767 civilians employed in three war industries located in the Philadelphia area. A 4 × 5-inch photofluorographic unit was employed. The diagnosis in positive cases was completed by a thorough physical examination, sputum studies, and a 14 × 17-inch roentgenogram. As a result of the survey, 1,633 persons (2.3 per cent) were classified as having x-ray evidence of reinfection tuberculosis. It was found that the incidence of tuberculosis increases with age, the percentage rising consistently from 0.3 per cent in the fifteen to nineteen-year age group to 9.4 per cent in the age group sixty-five and over. This holds true regardless of sex and race (white or colored). Cardiovascular abnormalities found incidental to the search for tuberculosis numbered 1,409, an incidence of 2.0 per cent. L. W. PAUL, M.D.

Pneumonia in the Aged. Analysis of One Hundred Sixty-Six Cases of Its Occurrence in Patients Sixty Years Old and Over. Frederic D. Zeman and Kaufman Wallach. Arch. Int. Med. **77:** 678–699, June 1946.

One hundred and sixty-six cases of pneumonia in men and women sixty years of age and older have been studied. In 143 of these (86 per cent), the clinical diagnosis of pneumonia was confirmed by roentgenography, fluoroscopy, or necropsy. Sixty-five cases were due to various types of pneumococci. Thirty-three cases (20 per cent) were fatal. One hundred and forty patients received sulfonamide drugs, 9 received penicillin, and 2 were treated with both drugs; 4 patients were given type-specific serum in addition to sulfonamide drugs. [These figures are taken from the text of the paper. They differ slightly from those given in the authors' summary.]

Among the conditions most frequently associated with pneumonia in the aged are cardiovascular, pulmonary, nutritional, and cerebral diseases.

Because of the obstacles to accurate physical diagnosis, roentgenography is of special value in these elderly patients, but even the roentgenogram may be misleading. In the differential diagnosis, the following diseases must be seriously considered and ruled out: (1) coronary thrombosis with myocardial infarct and early pulmonary edema, (2) congestive heart failure with or without pulmonary infarct, (3) pulmonary embolism arising often from a silent phlebothrombosis of the lower extremities, (4) pulmonary abscess, (5) bronchostenosis either from foreign bodies or from neoplasms, (6) pulmonary atelectasis of either the lobar (massive collapse) or lobular type, (7) pulmonary neoplasms, both primary and metastatic, (8) metastatic septic foci, (9) pulmonary tuberculosis, (10) bronchiectasis, and (11) the chronic lipid pneumonias. The principal complications are empyema, meningitis, and endocarditis.

The mortality in pneumonia in the aged has been dramatically reduced by recent advances in therapy. With earlier recognition of the disease, with proper appreciation of the complex problems encountered, and with better methods of treatment, still further improvement in the results may be expected.

Tularemic Pneumonia. Report of a Fatal Case. Ross Paull. California & West. Med. **64:** 346–348, June 1946.

Tularemia is an infectious disease caused by *Bacterium tularense*. It is transmitted by infected animals, ticks, and flies. Whether the disease can be contracted by inhalation is an unsettled question. The pulmonary form has been considered rare, but an increasing number of cases is being reported.

The symptoms of tularemic pneumonia may be mild, or the onset may be sudden and the course fulminating. Cough, fever (irregular and spiking), a relatively slow pulse, chill, diaphoresis, dyspnea, and prostration are common. In severe cases, cyanosis, delirium, stupor, and coma may occur. Roentgen findings vary with the type of the disease. Non-typhoidal cases usually show early hilar adenopathy with subsequent retrograde extension of the involvement through lymphatic channels to the lung parenchyma or even the pleura. The typhoidal cases, as a rule, present primary parenchymal involvement. Lung abscess, pneumothorax, pleural effusion, and residual fibrosis have been reported. Other aids to diagnosis are sputum studies, which may reveal the organism, agglutination tests after the first week of the disease, and animal inoculation.

The mortality rate has been reported as 40 per cent, bilateral cases having an especially poor prognosis. Therapy appears to be limited to symptomatic care, though some promising experimental results have been obtained with streptomycin (Heilman: Proc. Staff Meet., Mayo Clin. **19:** 553, 1944).

A case is recorded by the author, which he believes may have been due to inhalation of the organism. It was diagnosed as atypical pneumonia, its true nature being discovered only postmortem.

MAURICE D. SACHS, M.D.

Primary Atypical Pneumonia. A. B. Adams, G. L. Rolleston, J. M. Staveley, W. E. Henley, and J. E. Caughey. Brit. M. J. **1:** 227–231, Feb. 16, 1946.

The authors present a preliminary report dealing with the clinical, laboratory, and radiological data on 50 cases of primary atypical pneumonia occurring in the Naples area in 1945.

Fever, malaise, lassitude, and anorexia were present in all cases. Chills and sweating were present in over 50 per cent. Cough was present in 94 per cent. Headache was the most common neurological symptom. The sedimentation rate was moderately elevated. Eighteen cases (36 per cent) showed a positive heterophil antibody reaction. Increasingly positive cephalin-cholesterol flocculation reactions during the course of the disease were obtained in the majority of cases.

Positive radiological findings (parenchymal infiltration) appeared in the majority of cases from four to six days after onset of symptoms. Many infiltrations diagnosed as hilar in origin on the postero-anterior film were shown on lateral views to be in the apical segment of the lower lobe, and therefore to be peripheral rather than central lesions. No hilar adenopathy was noted. There were no instances of pleural effusion. Radiographic examination six weeks after onset showed complete resolution in the majority of cases.

[The positive cholesterol flocculation reactions and heterophil antibody reactions appear to be insignificant in such a small number of cases. Further data, as the writers suggest, would be needed to demonstrate the value of these tests in atypical pneumonia.]

ROBERT C. PENDERGRASS, M.D.

Bulla of the Lung. E. Robert Wiese. Dis. of Chest **12:** 238–241, May-June 1946.

Bulla is a pathological entity caused by the confluence of two or more terminal elements of the bronchial tree; it is the result of an increased intra-alveolar pressure sufficiently great to stretch or destroy the interalveolar walls. It is usually associated with a vesicular emphysema.

Bullae occur following conditions which interfere with the normal respiratory mechanism, as tuberculosis, silicosis, tumors of the lung or mediastinum, localized scar tissue or edema of a bronchus, areas of atelectasis or consolidation, and retention of heavy tenacious mucus within a bronchus. They are usually multiple, occupying those portions of the lungs which are most movable and least subject to continuous pressure from the chest wall, namely, the upper anterior and mediastinal aspects. They vary in size from a small vesicle up to 9 or 10 cm. in diameter.

A bulla of appreciable size is demonstrable on the roentgenogram as a localized area of rarefaction surrounded by a thin, sharply defined border, which is in sharp contrast to the heavy outline seen as a rule in cavitation due to tuberculosis or lung abscess. Bullae may be mistaken for spontaneous pneumothorax. In the latter condition one can usually trace the line indicative of the lung surface to the mesial side of the air space. Not only is this line likely to be denser than the line seen in a bulla, but in the majority of cases it courses toward the base of the lung, while that in bulla curves upward to merge with the pleural shadow in the axillary line or to form an oval, spheroid, or even lobulated, well-illuminated space. Bronchiectasis and congenital and acquired cysts may also simulate bullae.

A bleb differs from a bulla in that it occurs with interstitial emphysema, is formed by the rupture of an alveolar wall with subpleural escape of air, is movable under the pleura, and has no direct communication with a bronchus. HENRY K. TAYLOR, M.D.

Transient Pulmonary Radiologic Opacities and the Syndrome of Löffler. Cicero Michelangelo. Arch. di radiol. (Naples) **18:** 129–142, July-October 1942.

The author discusses the clinical and roentgenologic aspects of Löffler's syndrome and adds the observations of four physicians who had had it themselves.

E. T. LEDDY, M.D.

Pulmonary Disease Secondary to Cardiospasm, with Acid Fast Bacilli in the Sputum (Case Report). Emil Rothstein and H. B. Pirkle. Dis. of Chest **12:** 232–237, May-June 1946.

A white woman, aged 31, was admitted to a sanatorium with a diagnosis of bilateral tuberculous pneumonia. Sputum examination was repeatedly negative except for the discovery of acid-fast bacilli in three of eight concentrate specimens; it was subsequently decided that these were not tubercle bacilli. The roentgenogram showed "coarsely mottled conglomerate infiltration with multiple cavitation" in the upper half and "moderately coarsely mottled infiltration" in the lower half of the right lung. In the left lung there was a "conglomerate coarse infiltration, with multiple small cavitation, in the central lung field." The acute phase subsided, and the sputum thereafter was persistently negative, in spite of a profuse purulent expectoration. Further study revealed cardiospasm and a dilated esophagus. A review of the original roentgenogram showed a widened mediastinal shadow with a fluid level which had originally been overlooked. The acute pulmonary findings subsequently regressed and were replaced by a chronic fibrosing process.

The author believes that the roentgen picture obtained in this case may be characteristic, as exactly similar pictures have been described in two other cases (Warring and Rilance: J. Lab. & Clin. Med. **28:** 1591, 1943; Baldwin: Am. Rev. Tuberc. **45:** 756, 1942).

HENRY K. TAYLOR, M.D.

Pulmonary Oil Embolism. Maria E. Grossmann. Brit. J. Radiol. **19:** 178–180, May 1946.

Oil embolism in the lungs following uterosalpingography is fortunately rare. Several cases from this cause as well as other procedures involving the use of iodized oil have been reported. Two additional cases are presented here. In each the salpingogram was made to determine patency of the tubes. In one case the embolism occurred immediately after the injection and in the other two days later. In both cases the oil was demonstrable on films of the chest. Both patients recovered.

SYDNEY J. HAWLEY, M.D.

Pleural Transudates. Unusual Roentgenological Configuration Associated with Congestive Failure. Aaron E. Parsonnet, Emanuel Klosk, and Arthur Bernstein. Am. Rev. Tuberc. **53:** 599–607, June 1946.

Three cases are reported in which fluid collections developing in the pleural cavities as a result of cardiac failure did not show the usual roentgenographic signs of pleural effusion. In each instance the upper margin of the fluid shadow was sharply convex, simulating an elevated diaphragm. In two of the cases, the induction of pneumoperitoneum revealed that the abnormal shadows were above the diaphragm and fluid was aspirated. In the third case autopsy showed the true nature of the condition. In addition to roentgenograms taken in the supine and lateral decubitus positions to demonstrate shifting of the fluid, as recommended by Rigler, the authors suggest that pneumoperitoneum may also be a valuable diagnostic aid in cases of this type.

L. W. PAUL, M.D.

Mediastinal Tumors. Report of Cases Treated at Army Thoracic Surgery Centers in the United States. Brian Blades. Ann. Surg. **123:** 749–764, May 1946.

At the time of this report, 109 patients had been operated upon for mediastinal tumors at Army Thoracic Surgery Centers in the United States. This number includes only cases in which either the clinical manifestations of an intrathoracic neoplasm or discovery of a mass in the mediastinum by roentgen examination after entrance on active duty resulted in surgical exploration. There were 94 benign and 15 malignant tumors in the group.

Bronchiogenic cyst, considered to be a relatively rare growth, was encountered 23 times. An accurate preoperative diagnosis of this tumor depends almost entirely on roentgen examination. On the frontal projection, the mass may resemble a teratoid tumor or a primary nerve tumor. A lateral film is of more diagnostic significance, since the extreme posterior position common to most primary nerve tumors will not be duplicated, while the shadow of the mass on the lateral view is not usually so distinct as in the case of teratoid tumors. Fluoroscopy is also of importance in establishing the diagnosis; since most bronchiogenic cysts are attached to the trachea, the mass will move with the act of swallowing. Roentgenograms made by the Potter-Bucky technic, visualization of the esophagus with barium sulfate to determine its relationship to the mass, and delineation of the bronchial tree with radiopaque oil are sometimes useful. Unless the age and general condition of the patient preclude a major operation, the proper treatment of bronchiogenic cysts is surgical extirpation.

There were 20 *teratoid tumors* in the series. In 14 cases the tumor was benign. Far advanced malignant changes were evident in 6. Teratoid tumors usually produce sharp and obvious roentgenographic shadows, which are easily detected. Unless teeth or bone are visible on the films, however, the exact diagnosis cannot be made roentgenologically. The characteristic anterior position of the mass is suggestive but not conclusive. The relatively low incidence of teratoid tumors in military personnel is explained by the discovery of the tumor on the pre-induction roentgenograms of the chest. The treatment is surgical extirpation. Roentgen therapy is of no value in treatment of benign teratoid tumors and is probably equally ineffectual when malignant changes have occurred. The danger of malignant change is considerable.

Twenty-nine *benign neurogenic tumors* of the mediastinum, including neurofibromas, ganglioneuromas, sympathicoblastomas, etc., have been removed successfully. One patient with a neurogenic sarcoma was operated upon, but invasion of surrounding structures precluded removal. The roentgen shadow of a primary nerve tumor may be round, spherical, or lobulated. The typical extreme posterior position of the tumor is characteristic. Roentgen examination should include studies of the spine for bone erosion and evidence of so-called dumb-bell tumor. The shadow on the roentgenogram is usually sharply circumscribed, both in frontal and lateral views. The correct treatment is surgical excision before the tumor becomes malignant.

Roentgen therapy is futile in both benign and malignant neurogenic tumors.

Ten *pericardial cysts* are included in the series. Discovery of the tumor in each instance was by routine roentgen examination. Except for their anterior position, there is nothing characteristic about the roentgenologic appearance of pericardial cysts to differentiate them from other mediastinal cysts. Since surgical extirpation is the only means of establishing the benignity of a mediastinal tumor, operation should be recommended.

Six *tumors of thymic origin* have been studied. In 4 instances the lesion appeared to be benign. One patient with advanced myasthenia gravis was operated upon; a malignant thymic tumor was found and could not be removed completely. There are no definite criteria for the positive roentgen diagnosis of thymic tumors. One author has observed that in many cases the tumor has a tendency to maintain the shape of the thymus, as seen in roentgenograms of children. Another suggestive finding is that often the tumor is easily seen in the frontal projection but is not so apparent in the lateral view. Treatment may be either surgical extirpation or radiation therapy, depending upon the type of tumor.

Only 4 *mediastinal lipomas* have been removed. They have no distinctive roentgenographic features. Heuer and Andrus (Am. J. Surg. **50:** 146, 1940) predicted the true nature of a mediastinal lipoma in 2 cases because the shadow of the mass on the film became less opaque toward the periphery. This finding suggested to them that the tumor was composed of fat because it was more readily penetrable than the compact tissue of other tumors of the mediastinum.

The 14 *malignant tumors of the mediastinum* included 6 malignant teratomas, 2 thymomas, 1 neurosarcoma, 2 lymphoblastomas, and 4 cases of Hodgkin's disease. Except in 3 cases (all Hodgkin's granuloma), it was impossible to remove the tumor.

The role of radiation therapy in the treatment of mediastinal tumors is discussed. The author believes that the reluctance of physicians to recommend exploratory thoracotomy has probably resulted in the injudicious use of radiation therapy in many cases. Surgeons and radiologists experienced in thoracic disease should be able to predict in the majority of cases whether roentgen therapy will be successful. Even if errors in diagnosis occasionally result in thoracic exploration for tumors which will respond to radiation therapy, the danger to the patient from the operation is slight compared to the deleterious effects of prolonged and ineffectual irradiation. Most benign tumors of the mediastinum and some malignant neoplasms are amenable to surgical removal. Radiation therapy will fail to reduce the size or to halt malignant degeneration unless the tumor is of lymphatic origin. Moreover, after prolonged exposure to radiation, the removal of the lesion will be more difficult and hazardous.

Lymphomatous tumors of the mediastinum have a far greater tendency to produce clinical symptoms early, and their roentgen appearance is fairly characteristic. If, after a test dose of roentgen therapy, the neoplasm decreases in size, it can be assumed that it is of the lymphoma group, and surgical intervention is not indicated. Properly employed, radiation therapy is invaluable, both as a therapeutic and diagnostic measure. Friedman recommends an initial test dose of 750 r delivered to the center of the mass. It should be emphasized, however, that about one-third of malignant lymphomas will require as much as 1,500 r to affect the tumor. If, after a period of approximately one month, there is no change in the size of the tumor, thoracic exploration should be performed to determine the exact nature of the lesion.

A Method for the Orthodiagraphic Measurement of the Transverse Diameter of the Heart by Means of the Simple Fluoroscope. Frederick H. Howard. Am. Heart J. **31:** 724–727, June 1946.

The author describes a method for obtaining the true orthodiagraphic measurement of the transverse diameter of the heart with the use of the ordinary fluoroscope, without any orthodiagraphic attachments. This method is applicable only when the screen and tube move as a single unit. As aids, the author uses two triangular lead markers mounted on a tongue depressor (the apexes of the triangles are directed towards each other, and the bases are parallel and 10 cm. apart), an ordinary wooden applicator, a grease pencil, and a centimeter scale.

The tongue depressor with the lead markers is placed on the anterior chest wall, on a level with the second ribs, and is held in place with adhesive. If the chest is irregular in conformation, it may be necessary to bring forward one end of the tongue depressor by means of a wad of paper or cotton, since the lead markers must be equidistant from the screen. The wooden applicator is attached vertically to the center of the screen with adhesive. The screen must be held in one plane during the procedure, close to but not in contact with the chest wall. Lateral mobility of the screen is necessary.

Under fluoroscopic observation the distance between the upper angles of the lead markers is indicated on the screen. This distance divided by 10 equals the "magnification ratio," which is used as a correction factor for the subsequent measurements. The screen is moved so that the wooden applicator is tangential to the left border of the heart, and the lower angle of the right lead marker (i.e., right relative to the observer) is indicated on the screen by a short vertical line. This same procedure is repeated on the right border of the heart and the lower angle of the left lead marker is indicated by a short vertical line. The interval between the two vertical lines is measured, divided by the magnification ratio, and the result plus 10 equals the transverse diameter of the heart.

The logic for this procedure is discussed.

HENRY K. TAYLOR, M.D.

Congenital Anomaly of the Sternum—Vertical Non-Fusion. Report of Two Cases. Louis Gussow. Mil. Surgeon **98:** 420–424, May 1946.

Two cases of vertical non-fusion of the sternum are presented. Clinically the presence of an otherwise unexplained round scar-like depression in the upper midportion of the anterior chest accompanied by a skin fold suggests this anomaly. On forced inspiration with nose and mouth closed, a long, deep groove appears between the depression and the base of the neck, and on forced expiration, a large round bulge at the base of the neck. Palpation strongly supports this impression. A standard postero-anterior roentgenogram of the chest is not of much help. In an over-exposed film, however, a large central area of diminished density will be observed in the widened upper mediastinum. The exact nature of the anomaly is shown

by a roentgenogram of the sternum in the postero-anterior oblique position. The embryology of the sternum is discussed.

THE DIGESTIVE SYSTEM

Congenital Stricture of the Oesophagus. Richard Flynn. M. J. Australia **1:** 702–703, May 18, 1946.

A case of congenital stricture of the esophagus is recorded. The patient was seen at the age of ten years with a history of dysphagia since birth. A roentgenogram showed almost complete stenosis at the level of the arota, with extreme dilatation above. Esophagoscopy revealed only a pin-point orifice. Successive dilatations relieved the condition until a barium bolus of fair size could be swallowed. During the next three years dilatation was repeated at intervals and operation was then decided upon. This revealed aberrant veins crossing the esophagus, which appeared to be responsible for at least a good part of the trouble. Division of these veins and further dilatations were followed by improvement, and some months later the outlook was declared to be good.

The outstanding feature of this case is the obstruction due to aberrant veins, apparently springing from the azygos system. The report is a valuable contribution to our knowledge of esophageal stricture.

PERCY J. DELANO, M.D.

Isolated Hodgkin's Disease of the Stomach. Donovan C. Browne and Gordon McHardy. Gastroenterology **6:** 596–601, June 1946.

The authors add 2 cases of isolated Hodgkin's disease of the stomach to an estimated 20 previously reported. Roentgen examination of the stomach of their first patient showed indentations of the anterolateral aspect of the greater curvature, producing hemispherical filling defects in the cardiac region, with extensive mucosal irregularities. The proximal third of the stomach was fixed by adhesions. Peristalsis was sluggish. The patient died from massive gastric hemorrhage on the twenty-eighth day following gastrostomy. Autopsy revealed Hodgkin's disease involving the upper two-thirds of the stomach and the perigastric nodes. No other sites of Hodgkin's disease were found. The roentgen findings in the second case were so similar to those in the first that a diagnosis of lymphogranulomatosis was suggested, and this was confirmed at operation. The presence of sluggish peristalsis and the extensiveness of the roentgen defect, without a palpable abdominal mass, are notable features in these cases.

Megaduodenum Secondary to an Intrinsic Duodenal Diaphragm: Report of Case. Victor Drucker and Emanuel S. Cohen. Am. J. Roentgenol. **55:** 726–729, June 1946.

Congenital duodenal obstruction is discussed with particular reference to an intrinsic duodenal diaphragm. When the embryo reaches the age of five weeks, the lumen of the primitive gut is obliterated as a result of the proliferation of epithelial cells. Recanalization is soon effected, however, by the formation and coalescence of vacuoles between the proliferated cells, and the gastro-intestinal mucosa becomes histologically differentiated. The faulty recession of these cells is said to give rise to stenosis, atresia, and congenital diaphragm.

Duodenal diaphragmatic obstruction has been diagnosed at a wide variety of ages. Symptoms are present during the first two weeks of life in 38 per cent of the cases; in 10 per cent symptoms appear between the third and eighth month; in 24 per cent between the ages of one and eight years; and in 29 per cent after twenty-four years. The diaphragm has been reported as proximal to the ampulla of Vater in 45 per cent of cases; opposite the ampulla in 20 per cent; distal to the ampulla in 25 per cent; and at the duodenojejunal junction in 10 per cent. Microscopically the diaphragm is usually composed of mucosa and submucosa. Roentgen examination, with or without contrast media, will often reveal the dilated duodenal loop above the point of obstruction.

The authors present a case of intrinsic duodenal diaphragm, the ninth of this nature in an adult to be reported in the literature. The patient, a woman aged 23, was admitted to the hospital complaining of fullness of the abdomen for two days, with slight nausea but no vomiting or abdominal pain. Her history showed that two days after birth repeated projectile vomiting of clear, watery material had occurred. The vomiting diminished in intensity and frequency until the age of six years, after which it ceased altogether. Roentgenograms of the stomach, taken at the age of five years, were reported to show an abnormality of undetermined nature, for which surgery was recommended but refused. Physical examination on admission showed a soft, non-tender, tympanitic and distended upper abdomen. A gastro-intestinal series showed a somewhat enlarged stomach with tremendous dilatation of the first and second portions of the duodenum. In the region of the second portion the dilatation ended abruptly in a constriction, a few millimeters in diameter, below which the duodenum assumed normal dimensions.

At operation, a longitudinal incision was made through the constriction in the duodenum, revealing an intrinsic diaphragm with a central opening which barely admitted the tip of a Kelly clamp. The diaphragm was incised, and the longitudinal incision in the duodenum was closed transversely in order to widen the lumen at the site of obstruction. Two months after operation the patient was asymptomatic and stated that her upper abdomen had decreased in size. A gastro-intestinal series showed the duodenum to be of greater than average caliber, but considerably reduced as compared with the preoperative size.

H. H. WRIGHT, M.D.

Volvulus of the Sigmoid Colon: Discussion and Case Report. George C. Burton. J. Arkansas M. Soc. **42:** 251–252, May 1946.

The author believes that volvulus of the sigmoid colon accounts for 2 to 5 per cent of all hospital admissions for intestinal obstruction. It is the consensus of opinion that a redundant sigmoid with a long mesentery is a definite etiological factor. Constipation is said to be a contributing factor but, because of the prevalence of this condition, such a statement is hard to prove.

In the acute type the onset may be sudden, with severe abdominal cramps, fever, and leukocytosis. In the subacute type, which is more common, constipation and gradual distention of the abdomen usually precede the onset of cramps. As the obstruction nears completion, nausea and vomiting occur. Since the condition may be suddenly corrected by an enema, particularly if this is taken in the knee-chest position, it is always wise to question the patient on this point, as a history of repeated attacks may thus be obtained.

Examination will usually show pronounced abdominal distention, usually some diffuse tenderness, and absence of audible or visible peristalsis due to the fact that the huge gas-filled loop of the sigmoid colon rises high in the abdomen, overlying the active intestine beneath. Often the diagnosis can be made from a single flat film. Usually this will show an enormous dilated loop of what is obviously colon and some dilatation of the rest of the large bowel with gas. If a barium enema is given, there is likely to be complete obstruction in or near the rectosigmoid, while the termination of the barium column in the rectum is smooth in contradistinction to the irregular obstruction seen with carcinoma, which is the most important condition requiring differentiation. There is usually absence of gas in the small intestine.

The author describes the case of a 68-year-old woman with volvulus of the sigmoid of the subacute type, with symptoms present for several days before complete obstruction ensued. At operation a large segment of the sigmoid was found to be enormously dilated. A temporary colostomy as well as a sigmoidopexy was done. The colostomy was later closed and the patient was discharged in good condition. While treatment varies with different surgeons, there is general agreement that anything less than resection is inadequate.

BERNARD S. KALAYJIAN, M.D.

Action of Appendicular Extracts on the Motility of the Large Intestine: Radiologic Observations. Pietro Perona and Mario Rigon. Arch. di radiol. (Naples) **18:** 188–196, July-October 1942.

The study recorded in this paper was made with the view of obtaining information about the function of the appendix. After injection of 1 c.c. or of 2 c.c. of extract of bovine appendix (equivalent to 5–10 grams of fresh organ), the authors found in eight patients a more or less definite tonic effect on all the segments of the colon. This was rarely limited to the proximal colon. After a double dose (4 c.c.), the effect was more constant and more pronounced and of longer duration in twelve cases. The authors reproduce some roentgenograms in fifteen figures. Whether this study will have a practical clinical application remains to be seen.

E. T. LEDDY, M.D.

Proctoscopy and Barium Colon Study in the Diagnosis of Rectal Conditions. Isaac Skir. New York State J. Med. **46:** 1017–1018, May 1, 1946.

The author gives several case reports illustrating the fact that lesions in the rectosigmoid may be missed on barium enema examinations. He makes a plea that barium studies of the colon be preceded by digital and proctoscopic examination of the rectum. Use of the barium enema examination first may interfere seriously with visual examination and may engender a false sense of security in patient and physician.

ROBERT C. PENDERGRASS, M.D.

Spontaneous Gastro-Intestinal Biliary Fistulas. N. Frederick Hicken and Q. B. Coray. Surg., Gynec. & Obst. **82:** 723–730, June 1946.

The authors review 272 reported cases of spontaneous gastro-intestinal biliary fistulas and report 15 of their own operated cases. They state that these fistulas are not medical curiosities but occur in approximately 4 per cent of all patients requiring surgical therapy for disorders of the biliary tract. In 90 per cent of the reported cases, gallstones were the etiologic factor. Perforating peptic ulcers were the responsible agent in 6 per cent. Ulcers on the posterior surface of the duodenum usually perforate into the choledochus, while those on the lateral duodenal wall ulcerate through into the gallbladder. Gastric ulcers invariably involve the gallbladder. Cancer of the stomach, pancreas, gallbladder, and common bile duct produce a degenerative necrosis of contiguous viscera so that a variety of internal biliary fistulas result.

An analysis of 272 case reports shows that the gallbladder was involved in 88 per cent and the common bile duct in 11 per cent. The gastro-intestinal component consisted of the duodenum in 69 per cent, colon in 26 per cent, and stomach in 4.4 per cent.

When a fistula occurs, it either causes serious disturbances of the hepatobiliary system or it closes spontaneously. Generally a suppurative cholangitis, hepatitis, and obstructive jaundice result. The occurrence of a suppurative cholangitis, which is seldom observed in surgically produced fistulas, is explained by the presence of a concomitant choledochal obstruction, with resulting stasis of bile. Cholangiographic studies, performed on the operating table, confirm the presence of such obstruction and are of primary importance in surgical treatment.

Gastro-intestinal biliary fistulas produce no identifying signs or symptoms, but mimic the syndrome of the underlying condition. Symptoms are intensified with onset of the fistula.

Preoperative diagnosis depends entirely on the radiologist, but Borman and Rigler (Surgery **1:** 349, 1937) were able to make a correct radiologic diagnosis in only 37 per cent of 24 cases. Their review of the literature showed a preoperative diagnosis (in each instance by the radiologist) in 30 per cent of 267 cases. The demonstration of ingested barium, gas, or both, in any segment of the biliary tree is presumptive evidence of a fistulous communication. Most important is the finding of barium in the biliary radicles. The biliary and gastro-intestinal components can generally be recognized fluoroscopically. A relaxed sphincter of Oddi may occasionally allow biliary reflux, but here there is rapid elimination of the barium, while in the presence of a fistula the barium remains in the biliary system for six to twelve hours. Emphysematous cholecystitis may be differentiated by absence of reflux in barium meal studies. Acute intestinal obstruction due to migrating gallstones may occur and may be demonstrable on scout films or following the ingestion of a thin barium mixture. Cholecystocolic fistulas can usually be identified with the aid of a barium enema. If not, a double contrast enema may be necessary.

The authors emphasize the importance of adequate preoperative preparation and individualization in treatment. Cholangiographic studies made on the operating table are most useful, providing the surgeon with an accurate blue print of the problems confronting him. The primary surgical procedure is generally to effect free biliary drainage by choledochostomy before any major corrective procedure is attempted. The surgical procedures for the various fistulas are discussed. Prognosis is fairly good except in cases due to neoplasm.

JOHN A. COCKE, M.D.

Choledochus Cyst. Edward F. McLaughlin. Ann. Surg. **123:** 1047–1062, June 1946.

A case of choledochus cyst is presented. It is unique in that the patient was a Negro and that the diagnosis

was placed first among preoperative possibilities. Of the three "pathognomonic" signs of choledochus cyst—pain, tumor, and jaundice—the first two were present. Jaundice was absent both clinically and on laboratory examination. Roentgen studies confirmed the presence of the mass, revealed its cystic character, and showed that it contained gas. The inability to demonstrate a normal gallbladder suggested involvement of the biliary tract. Taking films with the patient in various positions was helpful in outlining the walls of the mass and in showing something of their nature—the failure to collapse in various positions, for instance. Identification of the air within the cyst was significant, and the fluid level indicated the presence and amount of liquid.

Gas in the gallbladder was visible on the films and, as described by the roentgenologist, "seemed to emerge from part of the tumor." Its full significance was not appreciated before the abdomen was opened. It should be looked for in future cases and may be regarded as a finding of utmost importance. Being isolated so exactly in the different views, the gas obviously was not within loops of the bowel itself; its constancy of position precluded its being free air under the diaphragm. The logical inference is that the gas in the cyst and that trapped in the gallbladder came from the intestinal tract *via* the communication between the cyst and the duodenum. Fluoroscopy, showing the duodenum crossing in front of the cyst, and roentgenograms showing the stomach from the side, containing barium which continued down in the duodenum in front of the cystic mass, were helpful. Of diagnostic value from the negative point of view was the fact that the gastro-intestinal and urinary tracts appeared roentgenologically normal.

The most plausible diagnostic possibilities, other than choledochus cyst, were pancreatic cyst, solitary cyst of the kidney, hepatic cyst, and "retroperitoneal" cyst.

Operation consisted in removal of approximately nine-tenths of the cyst and anastomosis of the remaining portion of the dome (that part into which the cystic and common hepatic ducts entered) to the duodenum. The postoperative course was uncomplicated.

Cœliac Disease: Survey from the Children's Hospital, Melbourne. G. E. M. Scott. M. J. Australia **1:** 659–665, May 11, 1946.

Celiac disease is a chronic disorder of early childhood characterized by the passage of large, pale, fatty, and offensive stools, accompanied by severe wasting and interference with bodily growth. It is not common, is seen among rich and poor alike, and is usually said to affect girls a little more frequently then boys. The author traces the history of the study of the disease from the original description by Gee in 1888 to the present. These patients are usually under five years of age, show great muscular weakness and tenderness, with a soft flabby feel to the flesh, have abdominal distention, are often anemic, and may show tetany and achlorhydria. There is usually no mental retardation, but epiphyseal development and growth are often deficient.

Pancreatic fibrosis and associated respiratory infection have been shown to be the etiological factor in some cases. In others, a similar clinical picture was evidenced with tuberculous involvement of the abdominal nodes. Still others show neither of these changes but may be attributable to a vitamin deficiency. In all there is apparent a definite disturbance in carbohydrate and fat metabolism associated in many with disturbance in the calcium balance.

Radiological studies of the small bowel were reported by May and McCreary (J. Pediat. **18:** 200, 1941) as showing tendencies toward "clumping" of the barium bolus in conjunction with low blood-sugar curves, but these findings were not considered diagnostic, being present also in disease of the pancreas, sprue, cretinism, infections, and occasionally in normal subjects. The disordered calcium metabolism frequently accompanying the disease may produce x-ray changes in the bones, such as delay in ossification and bony growth, transverse lines in the metaphyses, osteoporosis, osteomalacic deformities, celiac rickets, and dwarfism.

The author reviews 35 cases studied over a period of ten years. Twenty-three of his patients were males and 12 females. The average age of onset was two years and eight months. Six of the patients died, the average age being four years and eight months. Causes of death included toxic hepatitis, bronchopneumonia, thrombocytic purpura, acute gastro-enteritis with hemorrhage, pyelonephritis, and urethral calculus. Only one case is mentioned in which fibrocystic disease of the pancreas was found. Many of those who survived had moderate elevation of temperature over prolonged periods. No radiological evidence of rickets was found, but osteoporosis was observed. Many of the patients were below the average height and weight for their age.

BERNARD S. KALAYJIAN, M.D.

THE DIAPHRAGM

Congenital Hernia of the Diaphragm. Robert E. Gross. Am. J. Dis. Child. **71:** 579–592, June 1946.

Most congenital defects of the diaphragm can be repaired by surgical means. The present report concerns 7 cases, all successfully treated.

Most commonly, diaphragmatic hernias appear in the posterior or posterolateral portion of the left leaf. About 10 per cent of them have a true hernial sac which limits to some degree the extrusion of abdominal viscera into the chest.

Symptomatology depends on the extent to which the viscera are drawn into the chest and on the degree of lung compression. In the esophageal hiatus type, there is seldom much difficulty in infancy. Later, mucosal erosion may cause melena and anemia. Emesis, pain, or the signs of high obstruction may also occur. In one of the present series, there was herniation of an anomalous lobe of the liver into the pericardium.

The majority of cases of congenital diaphragmatic defects give severe symptoms shortly after birth. Cyanosis, vomiting, and physical signs dependent on the type and contents of the herniated structure are usually found. From a surgical point of view, the author believes that in most such cases the roentgenologist can supply all the necessary information from frontal and lateral views made with the patient upright. He considers fluoroscopic study after administration of a barium meal or enema superfluous, as information gained from such procedures does not alter the operative procedure and adds to the surgeon's difficulties. The size of the hernial mass, the state of lung compression, and the position of the heart are the main data desired by him.

Ingestion of a barium meal is advantageous, however, in cases of esophageal hiatal hernia. The length

of the esophagus, amount of stomach above the diaphragm, and presence of gastric of duodenal obstruction may be determined by this method.

In the rare case of herniation into the pericardial sac, angiocardiograms were employed to prove that the abnormal bulge of the cardiac shadow did not represent a dilated chamber. M. WENDELL DIETZ, M.D.

Para-Esophageal Hiatal Hernia. A Case Manifesting Gastrointestinal and Cardiac Symptoms and Presenting Itself on X-ray as a Mediastinal Tumor. Myron Herman and Emanuel Singer. New York State J. Med. **46:** 1020–1023, May 1, 1946.

The authors call attention to the fact that diaphragmatic hernia may produce pain similar to that of coronary disease. Their patient was a 53-year-old white man admitted for treatment of a minimal pulmonary tuberculous lesion and observation because of a recent coronary occlusion. There were few symptoms until the age of fifty, when attacks of substernal pain, together with an inverted T-wave in the electrocardiogram, led to a diagnosis of coronary disease. Unexpected improvement in the electrocardiogram with return of the T-wave to normal caused the cardiologist to suspect extracardiac factors. A rounded shadow in the lower mediastinum was found on barium examination to be due to herniation of a portion of the stomach.

ROBERT C. PENDERGRASS, M.D.

Primary Cystic Tumor of the Diaphragm. Orland B. Scott and Douglas R. Morton. Arch. Path. **41:** 645–650, June 1946.

To the 14 cancerous and 18 benign primary tumors of the diaphragm previously reported, the author adds a primary diaphragmatic cyst, of undetermined origin. Neoplasms of the diaphragm do not always produce symptoms and, when present, these follow no specific pattern. Roentgenography is of the greatest value in establishing a diagnosis and in differentiating between abdominal and intrathoracic masses. Intrathoracic tumors touching the diaphragm show motion synchronous with the normal respiratory excursion of the diaphragm. If the tumor lies underneath the diaphragm and protrudes through it into the thoracic cavity, a paradoxical movement of the tumor shadow is observed, similar to that characteristic of diaphragmatic hernia. The paradoxic movement of a diaphragmatic hernia may not be demonstrable, however, in the presence of adhesions within the hernial contents. Diagnostic pneumothorax is useful in differentiating lesions in the base of the lung. Pneumoperitoneum may aid in outlining the position of the tumor. Roentgen examination of the gastro-intestinal tract will rule out lesions involving the stomach or the bowel. When cystic tumors with calcified walls are encountered, intradermal or complement-fixation tests are indicated to exclude echinococcus cysts.

Details of the 32 previously recorded diaphragmatic tumors are tabulated.

THE MUSCULOSKELETAL SYSTEM

Juvenile Rheumatoid Arthritis (Still's Disease). James A. Coss, Jr. M. Clin. North America **30:** 568–575, May 1946.

The apparent differences in rheumatoid arthritis occurring in young persons (Still's disease) and in adults are due to the varying effect of disease processes in youth and maturity. As in adults, the disease in the young occurs more commonly in females. The highest incidence in children is between the second and third years of life. The pathologic findings are similar to those of adult arthritis. Muscle atrophy, however, is more marked and bony lipping or spurring is rarely seen; lymph node hyperplasia, splenomegaly, and hepatomegaly are more common. Myocardial, endocardial, and pericardial lesions similar to those of rheumatic fever are occasionally seen in juvenile arthritis. Adhesive pleurisy is a frequent finding in cases coming to autopsy.

Three types of localized skeletal change resulting from Still's disease, one or more of which are present in nearly 40 per cent of these cases, have been observed by the author: 25 per cent of the patients have an underdeveloped mandible (brachygnathia); 13 per cent have luxation or fusion of two or more cervical vertebrae; and about 10 per cent have abnormal shortening of one or more fingers or toes. These changes were observed in normal subjects with no growth disturbances prior to the onset of arthritis. The etiology of Still's disease, as of adult rheumatoid arthritis, has not been determined; certain predisposing factors are common to both groups.

Bone changes do not take place early and definite arthritis may be present without any significant roentgen manifestations. Regardless of the patient's age at the onset of rheumatoid arthritis, the earliest and most common finding is soft-tissue atrophy, swelling, or effusion. Next in frequency is decalcification, a decrease in bone density without loss of form. Joint-space narrowing or obliteration is seen only when the articular surfaces are damaged. Bone destruction also appears late and consists of localized loss of calcium, demonstrable roentgenologically as punched-out areas near epiphyseal lines. Some other features peculiar to Still's disease are: (1) the previously mentioned growth changes (brachygnathia, brachydactylia, and cervical fusion or luxation); (2) thickening of the periosteum on the shaft of metacarpals or metatarsals and phalanges, often giving a heavy appearance to these bones; (3) thinning of the shafts of phalanges, etc., occasionally giving a delicate appearance quite opposite to the above; (4) accelerated growth of epiphyses, resulting in a disparity in the length of the long bones.

Symptomatology, laboratory findings, and treatment are discussed.

Osseous Syphilis. Report of a Case. Mark Exley and A. W. Newton. New England J. Med. **234:** 661–664, May 16, 1946.

This is a report of a patient who complained of pain in his right arm and both thighs thirteen months after a rash. Kahn and Eagle tests were positive. X-ray examination showed destruction of the humerus between the mid and distal thirds, with periosteal reaction. In the lower left tibia there was a severe osteitis with bone erosion and periosteal elevation. The femurs showed proliferation, with erosion. Six months later, the right humerus was fractured by bumping it against a chair. Areas of decalcification were now demonstrable in the parietal and frontal bones. The ulnas showed periosteal elevation and bone destruction. The lesions previously observed had progressed. Treatment was now accepted for the first time. In four months there was marked improvement in the bones, with healing of the fracture, but unfortunately the patient failed to return after this.

The usual lesion in early syphilis is a periostitis. Osteitis is more frequent in early than in late syphilis. Pathological fractures are more commonly the result of neurosyphilis. The response to treatment is usually good in early syphilis of bone but not so in late syphilis. Radiographically the improvement depends upon the type of bone involvement. Proliferative change seldom shows improvement, while destructive lesions usually show bone regeneration. JOHN B. MCANENY, M.D.

Pulsating Benign Giant Cell Tumors of Bone. Report of a Case and Review of the Literature. Thomas A. Shallow and Frederick B. Wagner, Jr. Arch. Surg. **52:** 661–676, June 1946.

"Pulsating benign giant-cell tumor of the bone" is a benign type of tumor which, apparently as the result of free communication with large blood vessels, grows to a large size, pulsates, and occasionally yields a bruit. Because the physical signs simulate those of true arterial aneurysm, the lesion has been regarded as a form of so-called bone aneurysm. Although the comparatively rapid growth rate and large size of the tumor create a suspicion of malignancy, its benign character is demonstrated by the long survival and histologically by the absence of findings of hyperchromatism, mitosis, and other features of osteogenic sarcoma. There is nothing in the histologic findings, however, which differentiates pulsating and non-pulsating types of benign giant-cell tumor.

The differential diagnosis of the pulsating tumor is often exceedingly difficult. Telangiectatic osteogenic sarcoma, angioendothelioma, metastatic carcinoma, and hemangioma are other types of tumor which may show pulsation. Telangiectatic sarcoma usually occurs in young persons, grows rapidly, with destruction of the shaft of the bone leading to pathological fracture, and as a rule terminates in death from metastasis within a few months. Pulsating metastatic carcinoma usually results from a primary tumor in the kidney or thyroid, follows a slow course, and is generally found in middle-aged and elderly persons. Hemangioma and angio-endothelioma are usually found in adult and middle-aged persons, the former in almost any bone and the latter usually in the long bones. The radiological picture of hemangioma is often typical, showing the peculiar striations, which are vertical in the vertebrae. In all of these tumors the histologic picture is the best source of distinction.

The treatment for pulsating benign giant-cell tumors should be wide surgical resection. Radiation is usually only moderately effective. In the extremities the end-result is often an amputation. The prognosis for life is excellent.

To the six previously reported cases the authors add a seventh in which curettage followed by roentgen therapy to a lesion in the upper end of the tibia was unsuccessful, and amputation was eventually required.

LEWIS G. JACOBS, M.D.

Case of Raynaud's Disease with Osteopathy. Late Effect of Treatment with Marconi-Therapy. G. Fradà. Arch. di radiol. (Naples) **18:** 151–156, July-October 1942.

The author reports a case of Raynaud's disease of the hands with gangrenous ulceration, which did not respond favorably to ordinary treatment nor to peri-arterial sympathectomy. Roentgenograms of the hands are reproduced, showing the bony changes. A satisfactory result was obtained by the use of short-wave therapy applied to the cervicodorsal spine.

E. T. LEDDY, M.D.

Ruptured Intervertebral Disk Simulating Angina Pectoris. Allen Izard Josey and Francis Murphey. J. A. M. A. **131:** 581–587, June 15, 1946.

A ruptured lower cervical intervertebral disk frequently is associated with the anginal syndrome, the precordial pain simulating that of coronary artery disease. The nerve pathway for the production of this pain is unknown.

Seven cases of ruptured cervical disks are discussed. Operation had been done in three, with subsequent complete relief of precordial pain. The other patients were reassured concerning their cardiac status.

The authors conclude that all patients suspected of angina pectoris or coronary disease in whom symptoms, signs, and laboratory studies are inconclusive should be investigated for possible herniation of cervical nucleus pulposus. Differential diagnosis can be made on the basis of history, physical examination, electrocardiographic studies, and cervical spine roentgenography.

Lateral views of the cervical spine show straightening or a slight kyphos curvature replacing the usual lordotic curve, with acute forward angulation at the level of the ruptured disk in many cases. Narrowing of the intervertebral disk space may also be seen in the lateral projection. A reduction in size and alteration in shape of the intervertebral foramen may be noted in the oblique view. Localized arthritic changes may be present. An osteophyte may be seen projecting within the intervertebral foramen, representing calcification in the annulus fibrosus and the posterior longitudinal ligament over a perviously herniated nucleus pulposus.

H. D. WELSH, M.D.
(University of Michigan)

Spontaneous Dislocation of the Hip Joint. K. Lenggenhager. Schweiz. med. Wchnschr. **76:** 381–384, May 4, 1946.

It is well known that the hip may be dislocated after a purulent infection, but not so well known that similar dislocation may follow a sterile effusion, either primary or secondary to nearby inflammatory disease. The mechanism depends on the lessened effectiveness of the external atmospheric pressure and the muscular atrophy, which permit the femoral head to come out of the socket from behind forward, especially if the joint is held in semiflexion. The head is then able to move upward in response to normal muscle pull. Early diagnosis permits reduction with full recovery. The best prophylaxis is axial traction in abduction without flexion. Four illustrative cases are reported.

LEWIS G. JACOBS, M.D.

"March Fracture" of the Fibula in Athletes. Harry R. McPhee and C. Montanye Franklin. J. A. M. A. **131:** 574–576, June 15, 1946.

Six cases of so-called "march fracture" of the fibula and one of the foot, occurring in athletes, have been encountered by the authors. Early x-rays showed nothing or at most a suggestive haziness of the periosteum. Later, definite fuzziness, similar to that seen in periostitis, developed at a point along the bone and more frequently than not was accompanied by a doughy infiltration and swelling in the overlying soft tissues. A

definite fracture line with lateral radiations appeared in about four weeks. The process became sharply defined and subsided to a spindle-shaped swelling along the bone. The complete cycle of disability took ten to fourteen weeks, and attempts to modify the course by early immobilization were unsuccessful. The authors question the existence of a hidden "fracture-from-the-beginning" theory in view of the clinical picture in cases of known fracture, and believe that some other factor besides simple fracture is involved in these conditions.

Osteochondrolysis Circumscripta of the Astragalus (Osteochondritis Dissecans of König). Dino Agati. Arch. di radiol. (Naples) **18:** 143–150, July-October 1942.

Agati reports and illustrates two cases of osteochondritis dissecans involving the astragalus and discusses some points of clinical and roentgenologic differential diagnosis

E. T. LEDDY, M.D.

Significance of Minor Bone Injuries. H. W. Gillespie. Brit. J. Radiol. **19:** 173–177, May 1946.

In fractures, injury to the ligaments and other soft tissues is often of more importance in producing disability and delaying healing than the bony injury. The radiologist should always attempt to determine the extent of the ligamentous injury. Small flakes of detached cortex and chip fractures are indications of avulsion of the ligaments. The more usual sites for these injuries are the carpal bones, phalanges, tarsal bones, the elbow, shoulder, and ankle.

SYDNEY J. HAWLEY, M.D.

GYNECOLOGY AND OBSTETRICS

Evaluation of a New Contrast Medium for Hysterosalpingography. John B. Montgomery and Warren Lang. Am. J. Obst. & Gynec. **51:** 702–705, May 1946.

The authors have found visco-rayopake, which was introduced by Rubin in 1941, to be highly satisfactory for x-ray study of the uterine tubes. The outstanding advantage of this substance is due to the fact that it is well tolerated by the tissues and is rapidly absorbed from the peritoneal cavity. It was used to study the patency of the uterine tubes in 79 patients. The tubes were closed in 54 of this number; in the remaining 25, the medium flowed freely into the peritoneal cavity, where it was absorbed within thirty minutes.

Now that such a medium is available, gynecologists and radiologists need have no hesitancy in carrying out hysterosalpingography in all patients in whom uterotubal insufflation indicates obstruction.

F. B. MARKUNAS, M.D.

Roentgen Pelvimetry. J. N. Ané. New Orleans M. & S. J. **98:** 497–501, May 1946.

The Johnson method of stereoroentgenometry was used by the author for determining the pelvic diameters, because of its accuracy and adaptability to available equipment, and because it permits stereoscopic study of the pelvis. The Ball technic is recommended for cephalometry. These two procedures with sacral measurements complete the study of the individual case.

In a series of 1,767 cases the pelves were classified under three headings: normal, with normal or greater than normal diameters, 55.9 per cent; borderline, with contraction of 5 to 10 mm. in one or more diameters, 27.7 per cent; contracted, with 10 mm. or more contraction in one or more diameters, 16.1 per cent. The average normal pelvic diameters as determined by this study compare closely with those given by Williams. A valuable table shows the average diameters in the various types of pelvis according to the Caldwell-Moloy classification.

The author measures the posterior sagittal diameter of the inlet and midpelvis as well as of the outlet. He finds that this measurement at the inlet aids in the classification of the pelvis, and at the midpelvis helps to determine the amount of room present for turning of the fetal head. If the sum of the bi-ischial and posterior sagittal diameters at the midplane is less than 13.5 cm., difficult delivery may be expected. The minimal figure at the outlet is given as 17 cm., the sum of the intertuberous and posterior sagittal diameters.

Considerable attention is paid to the study of the sacrum. A line drawn from the promontory to the tip of the sacrum subtends the sacral curve and has been called the "chord." In this series, the chord varied from 7.8 cm. to 17.2 cm., with a mean of 11.5 cm. A perpendicular from the chord to the deepest portion of the sacral curve has been called the "sacral index." The average of this measurement has been found to be 2.2 cm. with variations from 0 to 5.9 cm. The sacral angle is measured at the intersection of the chord and the plane of the inlet; the average measurement is 72 degrees, with a variation from 51 to 98 degrees. The long straight sacrum set at a small angle to the pelvis has long been recognized as an obstetrical hazard. The well curved short sacrum in which the radius of the arc is too small to accommodate the fetal skull is another source of difficulty. The relationship of the chord, index, and angle of the sacrum should be considered in borderline cases, especially where an adequate posterior pelvis is essential for safe delivery.

The size and shape of the sacrosciatic notch determine the space available in the posterior segment of the inlet. In the android pelvis the notch is relatively narrow and angular at its apex. In the anthropoid pelvis the notch is relatively long and more curved. The platypelloid pelvis presents a notch similar in form but shorter than the gynecoid type.

The subpubic arch varies from the narrow angular form of the android to the wider curved arch type of the gynecoid pelvis. Its size and shape are closely related to the shape of the forepelvis and to the inclination of the sidewalls of the pelvis, which may be divergent, straight, or convergent. It is difficult to express the form of the arch in strictly mathematical terms. The inclination of the sidewalls should be considered with measurement of the bi-ischial diameter to determine whether contraction is due to large ischial spines or a narrow converging pelvic cavity.

The question of whether or not the baby can be born normally cannot be settled by x-ray studies alone, but only in combination with clinical examination and obstetrical judgment.

BERNARD S. KALAVJIAN, M.D.

THE GENITO-URINARY SYSTEM

An Estimate of the Value of Radiologic Examination of the Tuberculous Kidney. R. Hickel. J. de radiol. et d'électrol. **27:** 187–195, 1946.

This article on the radiologic study of the tuberculous kidney is well illustrated, with informative views show-

ing typical instances of destruction (beyond the "fringing" stage) in the upper poles, filling defects, dilatation of an infundibulum, contraction or stricture of a calyx, dilatation of a calyx (*dilatation en petale*), pyonephrosis, calcification, an abscess cavity communicating with a calyx, stricture at the ureteropelvic junction; also one case in which the filling defect simulated the appearance of a cystic kidney. Just to look at the illustrations is worth while as a review of the cardinal radiographic signs of renal tuberculosis.

PERCY J. DELANO, M.D.

Calyceal Diverticulum. E. R. Sterner, Harold O. Peterson, and Kano Ikeda. Minnesota Med. **29:** 578–581, June 1946.

This paper consists of a staff-meeting discussion of the little known condition "calyceal diverticulum." Five cases which are thought to illustrate this condition are presented, together with pyelograms. None of the patients has been operated upon, so the diagnosis was not proved in any case.

Pelvic Single Kidney: Report of a Case. Carroll D. Goodhope. Urol. & Cutan. Rev. **50:** 268–269, May 1946.

Thirty-six cases of pelvic single kidney have been reported in the literature to date. The authors add a case in which the ectopic kidney was demonstrated by pyelography. Transurethral prostatectomy was attempted, but postoperative complications resulted in the death of the patient. MAURICE D. SACHS, M.D.

Urinary Incontinence Due to Bilateral Ectopic Ureters. Laurence F. Greene and Deward O. Ferris. Surg., Gynec. & Obst. **82:** 712–716, June 1946.

Urinary incontinence due to an ectopic ureteral orifice is not common. The condition is most frequently unilateral, and the ectopic opening is usually associated with complete duplication of the pelvis and ureter. In most instances it is the opening of the ureter which leads from the upper segment of the duplicated kidney which is ectopic. Rarely an ectopic ureter may occur with a kidney which is not duplicated.

The orifices of bilateral ectopic ureters are most frequently situated in the urethra or vestibule of the vagina. The condition is much more frequent in the female, in whom the outstanding symptom is urinary incontinence, both diurnal and nocturnal. In the male, incontinence is usually absent and the condition is discovered following investigation to determine the source of a urinary tract infection.

If bilateral ectopic ureters are suspected, careful examination must be made of the urethra, vestibule, and vagina for the escape of urine from an ectopic orifice. It may be possible to catheterize the ectopic ureters and to secure pyelograms, as in one of the cases reported by the authors.

Excretory urography is valuable in the diagnosis. In most cases bilateral complete duplication of the renal pelves and ureters will be found, but those segments drained by the ectopic ureters will be visualized faintly or not visualized at all because their function is insufficient to concentrate the medium. In such instances, the diagnosis can be inferred from the fact that the visualized pelves (usually the lower) appear to occupy a low position in the soft-tissue outline of the kidneys. The presence of bilateral complete duplication of pelvis and ureter having been established, a diagnosis of bilateral ureteral ectopia can be made if but one ureteral orifice is situated at each extremity of the trigone.

Two cases are reported—one in a woman of twenty-six and one in a girl of nine. Complete cure of incontinence was achieved and normal kidney function maintained following bilateral heminephrectomy.

Illustrations are included to bring out the radiographic and anatomic aspects.

DAVID S. MALEN, M.D.

THE BLOOD VESSELS

Arteriographic Visualization of Cerebrovascular Lesions. Sidney R. Govons and Francis C. Grant. Arch. Neurol. & Psychiat. **55:** 600–618, June 1946.

This article consists of 11 brief case reports which illustrate the increasing importance of cerebral angiography in the diagnosis of intracranial lesions of vascular origin. Emphasizing the fact that the usefulness of the technic depends largely upon proper selection of patients and careful correlation of clinical and roentgenographic findings, the authors describe the neurologic and angiographic features of intracranial aneurysm, angiomatous malformations, occlusion of the internal carotid artery, and traumatic arteriovenous aneurysm.

Intracranial aneurysms usually are congenital in origin and the majority occur in the anterior portion of the circle of Willis. In the arteriogram the aneurysm appears as a saccular pouch adjacent to the artery from which it arises. The size of these lesions shows great variation.

Angiomatous malformations are congenital vascular defects in which large, dilated vessels are coiled into a tumor which resembles but does not actually represent a true neoplasm. These lesions usually occur along the distribution of the middle cerebral artery and present a striking angiographic picture.

Occlusion of the internal carotid artery may be due to arteriosclerosis, thrombosis, embolism, obliterating syphilitic arteritis, and non-syphilitic arteritis. Whereas clinical findings, plain roentgenograms of the skull, and encephalograms are seldom conclusively diagnostic, angiographic findings are characteristic. The internal carotid artery can be traced to the point of obstruction, and its cerebral branches are not visualized. If the patent vessel on the opposite side is injected, the vessels supplying both cerebral hemispheres can be seen.

Traumatic arteriovenous aneurysm implies the formation of a fistula between the carotid artery and the cavernous sinus or some other venous channel. Such lesions can be diagnosed in most instances by a bruit which may be audible to both patient and physician. Direct visualization of the lesion is readily obtained through angiographic examination

JOHN F HOLT, M.D.
(University of Michigan)

Thromboangiitis of Pulmonary Vessels Associated with Aneurysm of Pulmonary Artery. Report of a Case. L. E. Thompson and B. Gerstl. Arch. Int. Med. **77:** 614–622, June 1946.

An aneurysm of the right pulmonary artery, more than 10 cm. in diameter, which developed within a period of three months and was associated with thromboangiitis of both pulmonary arteries and veins, is reported Several features of this case are of particular

interest. The development of a large aneurysm in three months, without murmurs or palpitation, may be explained by assuming that the force of the flow of blood, while sufficient to expand the damaged arterial wall, engendered such velocity that the physical signs usually associated with saccular aneurysm were not produced. Various causes for the changes in the pulmonary vessels are considered. It is suggested that the condition described may represent a variety of periarteritis nodosa. If so, the unusual involvement of the larger pulmonary vessels would add a new feature to the already complex syndrome of periarteritis.

Translumbar Aortagraphy: Its Diagnostic Value in Urology. A. Keller Doss. J. Urol. **55:** 594–606, June 1946.

Translumbar aortography, though introduced by dos Santos more than fifteen years ago, has advanced little beyond the field of medical curiosity. The author has used the technic almost routinely in the study of renal disease during the past five years and believes that, with the development of a suitable non-toxic medium, it will become a standard procedure.

Since the foundation of an organ is dependent to a large extent on its blood supply, renal arteriography not only aids in the early diagnosis of pathological processes in the kidney but also offers a visual means of estimating its function. This knowledge is of great value especially from the surgical point of view, for often a large hydronephrotic kidney or the kidney filled with a staghorn calculus, considered fit only to be removed, may be found to be well worth saving. Congenital or acquired ectopia can be more intelligently and scientifically handled by means of aortography, since attenuation of the renal pedicle associated with pain and relative delay in emptying of the pelvis makes possible a correct decision with respect to nephropexy. This surgical procedure will therefore be employed less often and with a much higher percentage of satisfying results.

The author has found the study useful as an aid in the diagnosis of simple solitary cysts, hypernephroma, renal duplication, and in obstructions at the ureteropelvic junction due to aberrant vessels. In the presence of a retroperitoneal tumor, it is possible to exclude or convict the kidney in nearly every instance. The rare case of "Goldblatt hypertension" can be definitely established if obstruction or occlusion of one of the renal arteries can be demonstrated. Sixteen illustrations are included, showing how the renogram has been of aid to the author in the diagnosis and management of renal disease.

JOHN H. FREED, M.D.

Abdominal Aortic Aneurysm Simulating Perinephritic Abscess: Dorsolumbar Scoliosis. A Roentgen Sign of Aneurysm. Frederick B. Mandeville. Urol. & Cutan. Rev. **50:** 261–264, May 1946.

Demonstration of erosion of the vertebral bodies, with preservation of the intervertebral disks on a lateral roentgenogram, in association with a pulsating abdominal mass, is generally accepted as practically the only evidence of aneurysm of the abdominal aorta. The author reports 3 cases showing the classical findings on the lateral film and, in addition, a dorsolumbar scoliosis in the anteroposterior view, a finding which is usually considered highly suggestive of a perinephritic abscess. A number of cases of aneurysm simulating perinephritic abscess are cited from the literature.

MAURICE D. SACHS, M.D.

THE SPINAL CORD

Opaque Myelography in Penetrating Wounds of the Spinal Canal. C. L. Hinkel and R. L. Nichols. Am. J. Roentgenol. **55:** 689–709, June 1946.

World War II afforded the first opportunity for myelographic examination of considerable numbers of patients with penetrating wounds of the spinal cord and cauda equina. The authors employed this procedure in a large number of cases and found it useful in localizing and analyzing lesions and as a guide to surgical treatment. Patients with paralysis thought to be due to transection of the spinal cord or cauda equina were in many instances found to have surgically remediable lesions, and in some, operation several months after injury effected relief of the neurological symptoms. Thirteen of the patients in whom myelographic examination was done were operated upon, and correlation of the findings permitted evaluation of the significance of abnormalities seen in the myelographic picture. The major myelographic abnormalities encountered fitted into the following categories:

1. *Sharply localized, clearly marginated indentation.* This defect indicates localized external pressure on an intact dura. It was always found associated with fractures of and loose bone chips from the laminae or pedicles. With surgical removal of the bone fragments, the prognosis is good. The defect may be missed unless oblique or supine projections are used.

2. *Angulation* is the result of scarring and contraction of the dural and epidural soft tissues, or of traumatic unilateral severance of the nerve roots and the dentate ligament which normally stabilize the dural tube.

3. *Extra-arachnoid oil (near lesion).* Except when it is due to faulty technic, the presence of oil outside the subarachnoid space indicates a tear in the arachnoid.

4. *Displacement of the column of oil.* Dorsal or ventral displacement of the arachnoid contents may occur from anything which fills the subdural or epidural spaces. Lateral displacement has not been noted. The defect was found only in the presence of blood or blood clot between the dura and the bony neural canal.

5. *Feathery, irregular filling defects* (localized partial obliteration of the subarachnoid space) are due to pia-arachnoiditis.

6. *Altered physical characteristics of the oil.* When pantopaque is used, its dispersion into fine droplets has been found to be associated with alterations in the cerebral spinal fluid. Nearly all of these cases show high cerebral spinal fluid protein. Two cases showed xanthochromia.

7. *Complete subarachnoid block* may occur as the result of extrinsic pressure, intrinsic pressure, active inflammatory disease, or scarring as the result of very extensive destruction of nerve tissue.

The technical considerations are discussed in detail, and condensed reports of the thirteen cases are presented in table form.

H. H. WRIGHT, M.D.

TECHNIC

Two Mechanical Devices for Reducing the Risk of Radiation Exposure During Certain Types of Roentgen Examinations. B. J. Markman. Acta radiol. **27:** 388–391, May 6, 1946. (In English.)

The author describes new apparatus for distant manipulation of the contrast medium syringe in urethrog-

raphy and for the administration of the enema in examinations of the colon which reduce the radiation risk for examiner and assistants.

Girdle for Compression of the Ureter. Erik Lundström. Acta radiol. **27:** 385–387, May 6, 1946. (In German.)

The author describes a girdle-shaped contrivance for compression of the ureters during intravenous and retrograde pyelography. A gentle compression is obtained, without fixation of the patient on the examination table.

Radiologic "Chronocinography." Value of the Demonstration of Motion in Relation to Time. José Moretzsohn de Castro. Radiologia (Buenos Aires) **8:** 23–28, January-April 1945.

Brazilian Method of Clinical Cineradiography. José Jany. Ibid, pp. 29–43.

Contribution to the Cineradiographic Study of Gastroduodenal Motility. José Moretzsohn de Castro and Joao Ferreira. Ibid, pp. 44–49.

Contribution to the Study of the Physioradiology of the Small Intestine. José Moretzsohn de Castro and José Fernandes Pontes. Ibid, pp. 50–59.

These four papers are devoted to the cineradiographic technic devised by Jany and Moretzsohn de Castro of Brazil, called by them *cronocinegrafia radiológica*, and to its application to the study of gastroduodenal and small intestinal physiology.

RADIOTHERAPY

NEOPLASMS

Possible Progress in the Radiotherapy of Cancer (Neutron Therapy, Jolio Therapy, Alpha Therapy, Beta Therapy, Gamma Therapy, and Ultra-Gamma Therapy). Robert Coliez. J. de radiol. et d'électrol. **27:** 177–186, 1946.

This is an excellent article on nuclear physics and will be of special interest to anyone whose work leads him into this field, though the amount of higher mathematics which goes with a doctor's degree in physics is really a prerequisite to a complete comprehension of all the author sets forth. Nevertheless, those with the average physician's background in physics can get a great deal of substantial information from the paper. It contains a very clear exposition of the principles of Lawrence's cyclotron, and the diagrams in which the production of neutrons by the bombardment of beryllium by deuterons is shown are detailed and complete enough for any group of students in x-ray physics.

The theoretical pathways of ions struck off after collision of a neutron with an atomic nucleus are clearly drawn; the composition of body tissues in terms of the elements which may be fitted into these schematic representations is considered, and, even if one is not able to maintain his orientation while threading the mazes of Greek-letter formulae such as physicists and astronomers use, he may still gain a worth-while comprehension of the principles elucidated.

The formation of radioactive substances by neutron bombardment is fully considered and their possible therapeutic applications are discussed.

The description of the betatron is the clearest this abstractor has read. The author contrasts this instrument in several respects with the cyclotron, thereby elucidating the operation of each. One effect of the rays generated at betatron voltage is surprising and very interesting: according to present computations, the depth dose at 2 cm. will be about 200 per cent, at ten million volts; at fifteen million volts, the maximum will be found at 3 cm. and will exceed 250 per cent; at ten million volts, and at 10 cm. depth, the dose is expected to be about 500 per cent. The author points out, however, that the biologic phenomena cannot be anticipated, but must be observed, and that for this reason one should not be overimpressed by depth dose calculations. The atomic bomb is briefly mentioned.

PERCY J. DELANO, M.D.

Cancer in Childhood. I. G. Williams. Brit. J. Radiol. **19:** 182–197, May 1946.

The incidence of cancer in childhood as given by various authors ranges from 0.055 to 1.8 per cent. As a cause of death in children the disease assumes significant proportions. In 1939 the death rates for children under 15 in Massachusetts, were: 4.2 from cancer, 4.0 from pertussis, 2.7 from tuberculosis, and 1.3 from measles. Sarcoma is nine times as frequent as carcinoma in this younger group. In the British mortality tables cancer was not found under twenty-five years of age in the following sites: lip, tongue, mouth, esophagus, small or large bowel, rectum, gallbladder, pancreas, larynx, prostate, penis, scrotum, vulva, and vagina. The commonest sites are the kidneys and suprarenals, eyes, glands [lymph nodes?], muscle, bones, brain, and meninges, in the order given. After fifteen years there is a decrease in the incidence of tumors of the kidneys and brain.

In the series reviewed, numbering 181 patients, 8.3 per cent of the lesions were carcinoma and 91.7 sarcoma. Five of 15 patients with malignant epithelial tumors were alive and well, two having lived longer than five years. Of the 160 patients with sarcoma, 50 were alive and free of recurrence following treatment, 10 of these having passed the five-year period.

Surgical excision was the sole method of treatment in 37 cases, comprising parotid tumors, osteoclastoma, retinal glioma (excision of the eye), Wilm's tumor (nephrectomy), carcinoma of the breast, testicular tumors, ovarian carcinoma, and cerebral tumors. The operative mortality was 8.1 per cent.

Combined surgical removal and radiation was used in 66 cases, irradiation being done postoperatively. Radiation alone was used in 60 cases. The tolerance of the patient is limited by local tissue reactions and the constitutional response.

Because the normal tissues of children are actively growing, the difference between the lethal radiation dose for the cancer and for normal tissues is less than with adults. Accurate figures for the tolerance of the normal tissues are not available for different age groups. In general, infants tolerate 25 per cent of the adult dose and children 50 per cent. Where opposite parallel fields are used, the exit dose may be of significant proportions. The mucous membranes in children are closer to the surface than in adults and so will receive a relatively higher dose. The following general rules

were followed: small daily doses (100 to 150 r with back-scatter); no radiation on two days out of every seven; no patient under ten years given enough to cause a moist desquamation; patients over ten given 90 per cent and sometimes the full adult dose.

Constitutional effects of radiation are the same in children as in adults. Because of the closeness of the mucosa to the surface, as mentioned above, gastrointestinal disturbances are more apt to occur. A drop in the red and white cell counts may occur more suddenly and to a greater extent than with adults. Interference with bone growth may follow irradiation.

Several tables supply details of the cases constituting the series. SYDNEY J. HAWLEY, M.D.

Cutaneous Cancer from the Point of View of the Radiologist. William Harris. Arch. Dermat. & Syph. **53:** 586–587, June 1946.

Among the indications which will determine the type of treatment in cancer of the skin, the author mentions the life expectancy of the individual, location of the lesion and whether or not it involves cartilage or bone, the nature of the tumor bed, presence of scar tissue, and previous treatment. In persons whose life expectancy is short, cure is often sacrificed for palliative effect and thus radiation is used rather than surgery.

Cancers of the scalp and extremities and those resulting from x-ray burns and in other burn scars are best treated by surgery. The management of metastatic lymph nodes is also usually a surgical problem, although palliation and possibly cure may be obtained by radiologic means.

For single lesions up to 0.5 cm. in diameter one treatment of 3,000 to 3,600 r is used. For larger lesions the dose is five times 900 r (80 to 100 kv.) given in ten days. With contact therapy (45 kv., 1.2 mm. Al filter, 4.1 cm. focus-skin distance), six times 1,000 r is the dose. With this technic the rate of cure is over 90 per cent in cases not previously treated.

The invasion of cartilage is not a contraindication to radiotherapy, and there is no advantage in electrocoagulation or desiccation of the lesion before roentgen ray therapy. The author insists on lead cut-outs leaving 0.5 cm. of healthy tissue around the lesion as a necessity for a high percentage of cure.

JOSEPH T. DANZER, M.D.

Treatment of Cutaneous Epithelioma. George T. Pack. Arch. Dermat. & Syph. **53:** 576–585, June 1946.

There are no hard and fast rules in the treatment of epithelioma. A knowledge of the peculiarities of behavior of the various types of cancer, the limitations which the location of the cancer imposes and the advantages and disadvantages of each method of treatment are essential in obtaining a good result.

High-voltage roentgen rays, 200 kv. or more, are seldom used except for deeply infiltrating epitheliomas. As it is impossible to sterilize metastatic epidermoid carcinoma in lymph nodes by high-voltage irradiation alone, it must be supplemented by interstitial irradiation or surgical dissection.

Low-voltage roentgen rays (100 to 140 kv., 30 to 40 cm. target-skin distance, without filter or with 1.0 or 2.0 mm. Al, according to the thickness of the lesion) are of great value in the treatment of cutaneous cancer. The skin surrounding the lesion is shielded by 0.5 mm. to 1.0 mm. of lead. The lesions are treated by daily fractional doses of 250 to 350 r until a total dose of from 2,500 to 4,000 r is given. When small ports or cones are used there is little back-scatter; consequently the smaller the area the greater the irradiation required for a satisfactory result.

The Chaoul contact and Philips contact roentgen-ray therapy outfits are limited to a voltage of 50 to 60 kv. They operate at contact or at 3 to 5 cm. target-skin distance. For contact irradiation the output is about 800 r per minute; daily fractional doses of from 250 to 400 r are usually given to total from 3,000 to 8,000 r. The advantage of such apparatus is that most of the irradiation is absorbed by the tumor proper, leaving the deeper structures uninjured.

There are four standard radium applicators in general use at Memorial Hospital (New York). Their filtration is equivalent to 3 mm. of brass. They are applied at a distance of 1 to 3 cm. and their use is limited to superficial lesions. All epitheliomas which are more than 1 cm. thick and are more than 3 cm. in diameter should be treated by low-voltage roentgen therapy.

Whenever contact application of radium is desired over irregular surfaces a moulage of dental modeling wax may be used, in which radium tubes with 0.2 to 0.5 mm. platinum filtration are imbedded. The dose is computed on the basis of 75 to 100 millicurie hours per square centimeter treated. "Penetration of the radiating beam is very little and if the cancer is more than 5 mm. in thickness, supplementary interstitial irradiation should be employed or the radon or radium tubes should be implanted more deeply into the moulage to give a greater depth dose."

Radon seeds, 4 mm. long and containing 1 to 3 millicuries, find their chief application in the treatment of lesions of the ear, eyelid, and face. Care must be taken not to insert the seeds too near cartilage, or a painful perichondritis may follow.

Radon bulbs containing 300 to 600 millicuries of radon may be used for keratoses and small basal-cell epitheliomas, 200 to 600 millicurie minutes being given.

The author discusses the factors influencing treatment under five headings:

(1) *Location of Cancer:* A cancer in close proximity to bone or cartilage should be treated surgically. Any tissue that is difficult to restore by plastic reconstruction should be treated by low-voltage irradiation. The eyelids are best treated by low-voltage irradiation, with care to shield the eyeball to prevent cataract or iridocyclitis. The nose is also best treated by low-voltage therapy, the dosage being measured carefully to prevent a perichondritis or chondritis. For the ear and auditory canal low-voltage irradiation or contact radium by a moulage is preferred unless the cartilage is largely destroyed. The superficial insertion of gold radon seeds is used for cancers of the external auditory meatus. The skin over bony prominences of the hands and feet is poorly nourished and for this reason irradiation is not indicated in these locations. The only possible exception is when an epithelioma on the dorsum of the hand or foot is not of great thickness, in which event radium or low-voltage roentgen therapy may be used. Cancers of the sole of the foot should be treated by surgical excision as the skin will not tolerate injuries or weight bearing after irradiation. Late radionecrosis or recurrence often follows irradiation therapy of tumors of the scalp.

(2) *Type and Stage of Cancer:* The factors of fixation and infiltration are more important than histologic grading. In general, small basal-cell epitheliomas are

best treated by irradiation. Spindle-cell metaplasia of epidermoid carcinoma is so radioresistant that the surrounding tissue will slough from over-irradiation while the cancer cells still remain viable. A papillary carcinoma covering extensive areas should be removed by surgical endothermy and the base irradiated by fractional roentgen-ray therapy. Fixation is a contraindication to radiotherapy.

(3) *Recurrences:* When a cancer of the skin recurs after irradiation, further irradiation, as a rule, is not indicated. There is usually a loss of sensitivity and the surrounding tissue is more prone to radiation ulceration. If the recurrence is small, it may be treated by radon seeds.

(4) *Selection of Treatment of Cancers of Certain Types and Origins:* Bowen's disease should be considered a true carcinoma and the treatment should be the same as for squamous-cell carcinoma. Paget's disease should be treated as a carcinoma of the breast, with amputation. Cancer in acrodermatitis chronica atrophicans, xeroderma pigmentosum, lupus vulgaris, burns and scars, and in chronic radiation dermatitis should be treated by excision. When a cancer appears in a draining sinus, an attempt must be made to clear up the sinus. Therapy may then be given by the divided dose technic.

(5) *Treatment of Metastatic Carcinoma in Regional Lymph Nodes:* Radiation therapy alone cannot cure metastatic squamous or spindle-cell carcinoma. If the case is operable, dissection of regional lymph nodes should be complete. The factors for palliative irradiation therapy are 200 kv., 0.5 mm. Cu and 1.0 mm. Al, 50 cm. target-skin distance. Fractional doses are given daily—200 to 300 r until each port has received 2,000 to 3,600 r. JOSEPH T. DANZER, M.D.

Radiotherapy of Epithelioma of the Skin. Maurice Lenz. Arch. Dermat. & Syph. **53:** 588–596, June 1946.

Treatment of epithelioma of the skin by roentgen rays and radium is influenced by the accessibility of the growth and by its radiosensitivity. Most tumors of the skin are accessible to irradiation, as 98 per cent of basal-cell and 75 per cent of squamous-cell epitheliomas are located on the head and neck. Their curability decreases with the increase in size of the growth. The importance of radiosensitivity is best appreciated in the treatment of extensive epitheliomas, as smaller lesions are frequently over-irradiated and destroyed, irrespective of their inherent radiosensitivity. Adenocarcinomas and adenocystic epitheliomas arising in sweat glands are generally radioresistant and are best treated by surgery.

The radioresistance of the tumor bed is poor in poorly vascularized tissue; therefore, carcinomas arising in scar tissue should be treated surgically. Radiation damage to the tumor and the normal surrounding tissue is proportional to the amount of radiation and inversely proportional to the duration of treatment. The shorter the natural life cycle of the tissue irradiated the sooner will the radiation damage be recognizable. Thus mucous membranes will die and desquamate a few weeks after exposure but bone and connective tissue may not show irradiation damage for months. Osteitis or chondritis may develop from over-irradiation of lesions of the ear, nose, and scalp.

Metastasis to lymph nodes decreases the chance of cure from 54 per cent to 18 per cent. Surgery is preferable if the nodes are freely movable; roentgen therapy or the insertion of radium or radon seeds is preferable if the nodes are fixed.

The type of irradiation to be employed is influenced by the location and extent of the lesion, the radioresistance of the tumor bed, the blood supply, and the condition of the patient. Invasive epitheliomas may show a tiny surface tumor and a wide subsurface extension.

In contact roentgen therapy of superficial epitheliomas the target-skin distance is 1.8 to 4.1 cm., with no filter. For deeper epitheliomas 15 to 30 cm. target-skin distance is used, with 100 to 135 kv. and 3.0 mm. Al filter. For extensive lesions 130 to 200 kv. and 0.5 mm. Cu filter are usually preferred. In external radium therapy the target-skin distance is from 0.7 to 1.0 cm., in teleradium therapy from 6.0 to 14.0 cm.

If one hopes to cure an epithelioma, a single irradiation treatment is given by one or a series of exposures. If a cure is not expected, weak radiation intensities are repeated from time to time. A cancericidal dose for each variety of epithelioma has not been adequately determined. Whatever technic has been employed, correct irradiation should produce wet desquamation of the irradiated epidermis, leaving a denuded, raw, bleeding corium. The speed with which healing takes place depends on the size of the denuded area and the damage to underlying blood vessels.

In contact therapy, a single massive dose of 6,000 to 12,000 r may be given to superficial lesions 1.0 or 2.0 cm. in diameter, and good healing may result. Satisfactory results have also been obtained with 3,000 r (100 kv., 15 cm. target-skin distance) in basal-cell epitheliomas 1.0 cm. in diameter; 4,000 to 6,000 r, with doses of 250 r or 500 r every other day, leaves a better scar and is more effective. With 130 to 200 kv., smaller daily doses are given.

In external radium mold therapy, 4,500 to 7,000 r of gamma radiation are usually given. In interstitial therapy 4,000 to 7,000 r of gamma rays are given in from five to ten days.

As far as curability of the average epithelioma is concerned, it is immaterial whether one uses radiotherapy or surgical intervention, provided adequate treatment is applied to all cancer cells. Success depends on the appreciation of the extent of the growth and its adequate treatment during the first and only treatment.
JOSEPH T. DANZER, M.D.

Symposium: Malignant Melanomata. P. J. Moir, E. K. Dawson, Margaret C. Tod, Georgiana M. Bonser, I. G. Williams, and Frank Ellis. Brit. J. Radiol. **19:** 217–232, June 1946.

In his introduction to this symposium, Moir points out that in man pigment-containing cells are found in the skin, eye, and certain parts of the central nervous system. He classifies pigmented tumors as benign moles (congenital or acquired) and malignant melanomata. Between 65 and 80 per cent of malignant melanomata occur in pre-existing benign tumors or moles. Irritation is an important factor in the development of malignancy. The evidence of malignant change consists in a sudden increase in size, ulceration, bleeding, or the appearance of satellite tumors. Metastasis occurs early by both lymphatics and the blood stream. This may be explained by the fact that these tumors contain wandering phagocytic melanophores as well as fixed pigment-bearing cells. Because of the danger of metastasis, biopsy should not be done unless the lesion

is widely excised. Questionable lesions are better left alone.

Moir considers extensive surgical removal with block dissection of the regional lymph nodes the best treatment for malignant melanoma if the lesion is thought to be operable at all, and the other contributors to the symposium are in agreement with this view.

Tod reports a series of 107 cases of malignant melanoma (not all histologically proved), of which 23 had been treated radiologically at least five years earlier. There were 6 five-year survivals of this small group. She warns against radium implantation, except in the orbit, because of the trauma involved. Treatment by irradiation should always be by surface application and handling must be reduced to a minimum. After either radium mold or x-ray therapy, any sign of recurrence calls for immediate surgical removal.

Ellis, while admitting that in clinical practice complete proof that a malignant melanoma can be cured by radiation is rarely possible, believes that some of the lesions are undoubtedly radiosensitive. He presents results in 53 cases from the Sheffield Radium Centre, with four survivals of more than five years, though in no instance was there rigid proof of cure of a histologically proved melanoma.

Other points made in the course of the symposium include the following. Routine postoperative irradiation is not advisable for skin lesions. It is better to save the radiation for use to the limit of tolerance in known recurrences and metastases. Lesions on the head and neck give the best result probably because the more conspicuous position leads to earlier treatment. The disease is more certainly and rapidly fatal in younger subjects. SYDNEY J. HAWLEY, M.D.

Carcinoma of the Lip and Its Treatment by Radium (1928–44). Alexander A. Charteris. Brit. M. J. **1:** 719–721, May 11, 1946.

During the seventeen-year period, 1928–44 inclusive, 293 cases of cancer of the lip were seen at the Radium Department of the Western Infirmary, Glasgow. Forty-seven patients were not treated by radium for various reasons. The 246 cancers treated were not a selected group but included growths in all stages, with and without invasion of the lymph nodes, and some extending beyond the actual lip area. In the cases showing eventual failure, this was obvious by the end of the first year with but 7 exceptions, and for that reason all cases are included up to the year 1944, save 4 cases treated late in 1944 in which the outcome was doubtful. A total of 242 cases is thus left for analysis. All but 8 patients were males. In all but 8 cases, the primary lesion involved the lower lip; a secondary primary lesion subsequently appeared on the other lip in one upper-lip and two lower-lip cases. Thirty-four patients had secondary involvement of the lymph nodes when first seen; of the 208 cases with no obvious involvement of the cervical nodes, although the neck was not treated, only 19 (about 9 per cent) had cervical metastases at a later date. The policy with lip cancers has therefore been to treat the primary growth and rely upon the routine follow-up to detect any regional metastases. Surgery and implantation of radium show the greatest promise in the treatment of cervical nodes.

Implantation of radium was carried out in 120 patients without lymph node involvement; 117 of these (97 per cent) were free of disease at the time of the report. In 6 of this number a residue or small recurrence had been excised. The needles employed for implantation have a linear intensity of 0.6 mg. of radium element per cm. of active length; those with a total length of 44 mm. (2 mg. Ra el.) and 32.7 mm. (1.2 mg. Ra el.) have proved most useful. Two common arrangements were a 4.5 × 2-cm. rectangle (three 2 mg. Ra el. closed at each end by a 1.2-mg. needle) and a 5.5 × 2-cm. rectangle (six 1.2-mg. needles in tandem pairs, closed at each end by a needle of the same strength). The strength of each line is uniform so that the dose rate rises toward the center of the area, but the results from every point of view have proved so good that no adjustment has been made. The dose delivered 0.5 cm. from the needle plane in 168 hours varies between about 5,000 r and 6,000 r, with a maximum of 6,700 r toward the center. At the extreme corners of the rectangles the dose falls to about 4,000 r but, with the margin provided, this part is not in the tumor zone.

Fifty-five patients without regional metastases were treated with double radium molds. Forty-eight (87 per cent) were free from disease at the time of the report, 3 having had excision of residual tumor or small recurrences. A dental apparatus is used in a form suitable for irradiating the inner and outer surfaces of the lip simultaneously. With a radium-mucosa distance of 0.5 cm. and radium-skin distance of 1.0 cm., about 6,000 r is given throughout the lip; the mucosal dose is higher than this, but no untoward results have ensued.

In 14 patients without involvement of the nodes, the cancer was first excised and radium then applied. There was one failure in this group.

Among the 34 patients with regional metastases when first seen there were 19 failures and among the 19 with secondary involvement developing after successful treatment of the cancer of the lip, there were 9 failures.

Sixty-seven patients showed some definite evidence of scarring, with or without telangiectases, following irradiation. Actual tissue damage in the form of late necrotic ulcers was seen in 6 patients, but 4 of these were treated in 1929–31, when no physical control was possible. Five of these had been treated by implantation. Healing occurred in all, with some scarring. In no instance did the necrotic lesion exceed 1.0 cm. in diameter, and the lip was never perforated.

Cancer of the Larynx and Pharynx. Results of Radiation Therapy at Charity Hospital. Manuel Garcia, Joseph V. Schlosser, and Joseph B. Marino. New Orleans M. & S. J. **98:** 483–489, May 1946.

The authors review the results of radiation therapy in 88 histologically proved cases of a series of 104 cancers of the larynx and pharynx seen by them in the Charity Hospital, New Orleans, in the years 1939 to 1942, inclusive. All but 3 of the 88 patients were traced. Those lost to follow-up were counted as dead, and those who refused treatment or were too ill to receive it were considered as radiation failures. The results thus represent the minimum accomplishment of radiation therapy in consecutive cases demonstrated histologically.

Topographically, the lesions were distributed as follows: rhinopharynx, 6; soft palate, 12; tonsil, 14; vallecula and base of tongue, 13; aryepiglottic fold, 7; piriform sinus, 6; lateral and posterior walls of pharynx, 10; ventricular band, 7; ventricle 1; vocal cord, 11; subglottic region, 1. Symptoms were dependent upon the site. Severe constitutional effects, with loss of weight, anemia, and fever from tumor sepsis or pul-

monary complications were present in many of the cases when first seen.

The authors believe that these patients should have as complete a diagnostic survey as possible to provide a sound basis for a rational plan of treatment. They recommend particularly laminagraphy combined with lateral roentgenography to determine the extent of involvement.

The presence and extent of cervical metastases affect the chances of recovery in a decisive manner. In this series, 43 per cent of the patients had metastases on admission, and in others they developed subsequently, so that a total of 57 per cent had metastatic involvement at some time in the period of observation. No radical dissections were performed. The percentage of salvage in this advanced group is smaller than in cases more suitable for surgical treatment, but of 19 patients with metastases treated over five years earlier, 3 remained well.

Irradiation is by the Coutard technic (protracted fractionation). This, the authors warn, must be considered a radical therapeutic procedure, not to be undertaken without careful study and preparation of the patient. The tolerance of the normal structures must be reached. Sharp reactions must be obtained, and the discomfort may be so pronounced as to affect the patient's general condition. The main factors to be taken into consideration are the volume of tissue to be subjected to high dosage and the rate of administration of treatment. With careful study of the physical problem and continuous clinical observation, the treatment can be executed with little risk of serious injury. The authors have aimed at delivering a tumor dose of 4,400 r ±10 per cent in a period of thirty days when the area of treatment ports does not exceed 50 sq. cm. A somewhat lower dose must be used with larger areas. In some locations, notably the rhinopharynx, intracavitary radium therapy may advantageously supplement roentgen therapy. Interstitial radium implants may also be helpful in carcinomas of the vallecula, the base of the tongue, the tonsil, and metastatic cervical nodes. The implant is done in a single or double plane and the tissue dosage is between 3,000 and 6,000 gamma roentgens.

All cases included in the series studied were inoperable either for technical or clinical reasons. The overall survival rate was 24 per cent at three years. Patients with lesions of different histologic type showed varying survival rates but the authors felt that the number of cases involved was too small to make the variations significant. The more immature carcinomas showed a better result, and adenocarcinomas responded well to treatment, indicating that they are not necessarily radioresistant. No significant racial differences were noted. Better results were observed in women, though they represented less than one sixth of the total number of cases. Patients with no metastases at any time showed 36 per cent three-year cures while those with metastases on admission showed only 13 per cent.

Only 77 of the patients completed the treatment course. None of the others survived as long as one year and the same is true of those who did not obtain primary healing whether with full or incomplete treatment.

It is believed by the authors that in unselected material, only about 60 per cent receive tangible benefit in the form of freedom from symptoms and longer survival with present methods of treatment. They believe it is important to establish objective criteria for judging suitability for radiation therapy before it is instituted, similar in nature to the criteria of operability. So far, no facts have been elicited which would enable them to foretell the response to radiation therapy in a given case. The factors most suggestive of a favorable response are limited anatomic involvement, preservation of mobility of normal parts, and a papillary architecture of the tumor. Good results have been obtained, however, in the absence of all these criteria, and every patient should be given the benefit of a trial of radiation, at least until more definite criteria for selection are established.

Once primary healing had been achieved, late failures occurred as the result of local recurrence in 34 per cent of the patients, as a result of metastases in 22 per cent, and of intercurrent disease in 4 per cent, while 40 per cent remained alive and well at the end of three years. In regard to localization of the disease, 31 per cent of 32 patients with upper pharyngeal involvement survived three years, 11 per cent with lower pharyngeal involvement, and 35 per cent with endolaryngeal involvement. These results are similar to those obtained elsewhere. Among 47 cases observed over five years, the corresponding percentages were 28, 7, and 21. The low survival rate with involvement of the lower pharynx indicates the need for improvement in the method of treating those cases.

BERNARD S. KALAVJIAN, M.D.

Cancer of the Breast: Statistical Report of Results. Donald V. Trueblood. West J. Surg. **54:** 217–227, June 1946.

This report is based on 65 breast carcinomas all treated surgically. No preoperative or postoperative radiation therapy was used. The author does not believe that sufficient radiation can be given to eradicate the disease; and then, too, he believes there is too long a delay following irradiation before surgery can be done. As to postoperative irradiation, if surgery has been complete this is not indicated; if cancer remains, its location cannot be determined and radiation cannot be given in sufficient amounts to the entire field.

Forty-four (67.7 per cent) of the author's 65 patients survived four years or more; of 26 without axillary involvement, 23 (88 per cent) survived five years; of 38 with axillary involvement, 50 per cent survived for five years.

MAURICE D. SACHS, M.D.

Evolution of Radiotherapy with Radioactive Substances for Carcinoma of the Breast. V. Palumbo. **Radiodosimetry—Radium Therapy with Molds in Carcinoma of the Breast (Note 2).** M. Paoletti. Arch. di radiol. (Naples) **18:** 157–187, July-October 1942

After a review of the literature on the value of preoperative and postoperative radiotherapy for carcinoma of the breast, the authors present charts showing the distribution of energy in the breast and its lymph-drainage areas by their technic of surface application of radium and x-rays and describe the clinical doses they have given to 111 Stage 2 cases. By this combined method they obtained satisfactory results, that is, a five-year survival rate of 61.2 per cent, a six-year survival rate of 45.4 per cent, and seven-year survival rate of 31.5 per cent. The indications, contraindications, technic, and skin reactions are discussed in some detail.

E. T. LEDDY, M.D.

Prognosis and Problems in Renal Tumors. Clyde L. Deming. J. Urol. **55:** 571–582, June 1946.

The author discusses the prognosis and problems associated with renal neoplasm and reports a series of 82 cases which were carefully followed.

In general 95 per cent of renal tumors are malignant. The usual five-year survival is 20 per cent but it is to be noted that many will die of metastasis before a second five years has elapsed.

In the author's series of 82 cases only one was lost from follow-up and that after a survival of over ten years. It was noted that two periods of life showed a relatively high incidence of renal tumors, the first decade and the later decades: 13.4 per cent of the 82 cases were in the one to ten-year age group. It was also noted that 72 per cent of the tumors occurred in males and that in two-thirds of the cases the right kidney was affected. Since he considers the terminology of renal tumors chaotic, the author has not classified his cases on a pathologic basis. His results were comparable with the generally reported results. At the end of five years 19.5 per cent were living. At the end of ten years 14.6 per cent were living but only 9.08 per cent were free from metastasis.

The use of irradiation is discussed but no definite conclusion is reached. "Certainly," the author writes, "x-ray irradiation should never be given until a histological diagnosis is made and then with reservation. . . . So far we have no specific means to designate radisensitive and radioresistant renal tumors."

FREDERICK A. BAVENDAM, M.D.

Roentgen Therapy for Malignant Teratoma of the Testis. Raymond J. Scheetz and Eugene T. Leddy. Am. J. Roentgenol. **55:** 754–764, June 1946.

There has been considerable confusion in the literature regarding testicular tumors because of differences in classification. Some believe that all of the common tumors of the testis are teratomatous in origin. Others feel that seminoma, at least, is a different and distinct entity. The authors, following Broders' classification, adhere to the latter view. They point out that the tendency, when computing survival rate, to group all varieties of tumors of the testis together, has made it impossible to determine to what extent irradiation has been of value in each variety.

This report is based on 54 cases of histologically verified malignant teratoma of the testis. The incidence, etiology, pathology, site of tumor, symptoms, diagnosis, and therapy are discussed. The maximal incidence of teratoma occurs earlier in life than that of seminoma. Ninety-three per cent of the patients were between fifteen and thirty-nine years of age. A painless swelling of the testis was the most frequent initial symptom. Pain was the prominent symptom in 16 cases. The most frequent sites of metastasis were the para-aortic lymph nodes, supraclavicular nodes, peribronchial lymph nodes, inguinal lymph nodes, and skeleton.

Tests for urinary gonadotropin were not used and are considered to be of decidedly limited value. Histologic examination affords the only means of accurate diagnosis. The authors favor immediate surgical excision of the tumor on diagnosis rather than the use of preoperative roentgen therapy.

The results obtained in 36 of the authors' cases are analyzed. In 17 of these cases treatment was begun when there was no evidence of metastasis. It consisted in simple orchiectomy and postoperative roentgen therapy. Eight patients lived five or more years after operation. Of the remaining patients who had clinical evidence of metastasis when treatment was begun, none was alive after five years. Only one of these lived three or more years after operation (40 months), and roentgen therapy was not begun on this patient until 32 months after orchiectomy. The dosage and method of application of the roentgen therapy are not stated.

The authors conclude that roentgen therapy does not appear to have any beneficial effects on malignant teratoma of the testis. H. H. WRIGHT, M.D.

A Case of Sarcoma of Bone Treated by Radiotherapy. Gwen Hilton and L. E. Glynn. Brit. J. Radiol. 19: 198–202, May 1946.

An interesting case is reported of an osteogenic sarcoma in the femur of a man twenty-six years of age, with treatment by radiation only. The patient sustained a fracture of this femur in an air raid ten years later. As the fracture failed to unite, the leg was amputated. Examination of the amputated limb showed the cortical bone to be thinned. The endosteal surface was extremely roughened. There were pseudo-cysts filled with white gelatinous material in the cancellous bone of the head and the greater trochanter. The medullary cavity was filled with a rich network of hard bone, the interstices of which contained opaque, white fibrous tissue. The cortex distal to the fracture was perforated in several places, the perforations filled with opaque, white, dry, crumbly material.

Microscopic examination showed the cortical bone to to be replaced by a layer of close-meshed cancellous bone with loose, moderately cellular and vascular fibrous tissue filling the marrow spaces. The haversian system was present, but the marginal lamellae were completely absent. Some of the haversian canals were filled by basophil lamellae indicative of a sclerosing process. The periosteum was virtually acellular and avascular. Many of the bone lacunae were swollen and empty. The medullary cavity was filled with an elaborate network of spongy bone with the interstices containing poorly cellular and poorly vascular connective tissue. There was no osteoblastic nor osteoclastic activity but many trabeculae were undergoing an apparently acellular central disintegration and surface erosion. There was no evidence of sarcoma.

SYDNEY J. HAWLEY, M.D.

Roentgen Therapy of Benign Giant Cell Tumor of Bone. Simeon T. Cantril and Franz Buschke. West. J. Surg. **54:** 259–264, June 1946.

The authors report two cases of giant-cell tumor of bone which responded excellently to irradiation. They consider roentgen therapy of such tumors highly satisfactory. Surgery should be considered only if the resection is to extend beyond the tumor area or if it will expedite the end-results, as in the head of the fibula. Curettage is unsatisfactory because of recurrence and danger of infection. The main problem in giant-cell tumors is the correct roentgen diagnosis (biopsy should not be necessary) and avoidance of over-irradiation. Therapy should be given in such a way that a minimal lethal tumor dose is delivered without interfering with bone regeneration. MAURICE D. SACHS, M.D

Leukosarcoma. Franklin B. Bogart. Am. J. Roentgenol. **55:** 743–753, June 1946.

Under the title "Leukosarcomatosis" Sternberg in 1908 described a group of cases characterized by marked mediastinal enlargement, including the thymus gland, and a terminal blood picture usually classified as an acute lymphatic leukemia. Other features of the condition are enlarged superficial lymph nodes and lymphoblastic infiltration of various organs of the body, particularly the thymus, liver, spleen, and kidneys. Biopsy of a lymph node is usually reported as showing lymphosarcoma. At the onset of symptoms the blood picture may be normal. The predominant blood cell in the terminal phase is usually described as a lymphoblast. Isaacs believes that the cell is a characteristic one which can be differentiated by staining properties, and he designates it as a leukosarcoma cell. Some authors include cases in which the predominant involvement is elsewhere than in the mediastinum.

Respiratory distress is frequently the first symptom. Other symptoms reported are malaise, weight loss, slight elevation of temperature, bleeding, joint pain, herpes, toxic erythema multiforme, diplopia, and local edema.

The mediastinal tumors are markedly radiosensitive, and roentgen therapy is indicated when there is circulatory or respiratory distress. Prompt reduction in the size of the tumor and relief of the distress may be obtained after administration of 200 r to 400 r, but roentgen therapy does not influence the ultimate course of the disease, which usually terminates fatally in a few weeks to a few months.

The author reports in detail two cases which conform to Sternberg's description of leukosarcoma. The reports include the clinical, laboratory, roentgenologic, and autopsy findings. The first patient received no roentgen therapy. The second received roentgen therapy to the mediastinum with dramatic relief of respiratory symptoms but survived for only a short period of time. In both patients a leukemic blood picture appeared before death, indicating that roentgen therapy is not the cause of change from a normal to a leukemic blood picture in these cases.

H. H. WRIGHT, M.D.

Leukaemia Treated with Urethane Compared with Deep X-Ray Therapy. Edith Paterson, Alexander Haddow, Inez Ap Thomas and Jean M. Watkinson. Lancet **1:** 677–682, May 11, 1946.

Urethane (ethylcarbamate) was used in 32 cases of leukemia (19 myeloid, 13 lymphatic), and the patients were observed over periods ranging from five weeks to eleven months. The condition of 15 of the patients was considerably improved: 7 of this number received urethane only; the others also had some x-ray therapy. In 9 cases, there was some improvement, but it was not considered satisfactory; 5 of these patients received urethane only. Of the 8 patients who died, only one had received x-ray therapy. Six of the 32 patients had blood transfusions. For purposes of comparison, a group of 31 patients with myeloid leukemia and 14 with lymphatic leukemia treated by x-ray therapy were studied. The effects of urethane and of deep x-ray therapy are strikingly similar. In the favorable cases there was a fall in the total white-cell count to normal limits, with a tendency for the differential count to approach a more normal pattern, diminution in the size of the spleen and enlarged lymph nodes, and a rise in the hemoglobin level. There is no indication that permanent benefit may result from the use of urethane in either myeloid or lymphatic leukemia, for relapses take place and immature cells may reappear in the blood. The cases are too recent to enable any statement to be made about the effect of treatment on length of life. The palliative effect, however, in many cases was great. Because oral administration of urethane produced nausea and vomiting in a considerable number of cases, the drug was given by rectum.

Urethane was also administered in 13 cases of advanced cancer of the breast and 11 cases of lymphosarcoma, Hodgkin's disease, and recurrent mixed salivary tumor of the antrum. A moderate leukopenia was observed in 9 of these. In 3 of the breast cases and 4 of the miscellaneous group there was a temporary diminution in the size of the lesions.

NON-NEOPLASTIC DISEASE

Treatment of Rheumatic Fever by Roentgen-Ray Irradiation. Geo. C. Griffith and E. P. Halley. Ann. Int. Med. **24:** 1039–1042, June 1946.

Two hundred and one patients, all of whom had a well established rheumatic fever of six months or more duration, were studied in the Rheumatic Fever Unit, at the U. S. Naval Hospital, Corona, Calif. Before roentgen therapy was instituted, a careful evaluation of the history, physical findings, and laboratory studies was made for each patient. A similar evaluation was made at the end of twelve weeks, and 42 patients were again evaluated at the end of twenty-six weeks. Weekly electrocardiograms and blood sedimentation rates were recorded.

The 201 patients were divided into three groups on the basis of treatment, but neither the roentgenologist, the clinicians, or the patient knew in which group any individual was placed by the technician. *Group A* received 100 r through the myocardium at weekly intervals for five successive weeks. *Group B* received 100 r through the myocardium and over the middle and lower cervical sympathetic ganglia at similar intervals; *Group C* went through the same mechanical routine but a lead filter was used to block out the roentgen rays, so that no radiation was received. Neither after twelve weeks nor after twenty-six weeks were any significant differences observed in the three groups, from which it is concluded that roentgen therapy is not a useful procedure in rheumatic fever.

Levy and Golden had previously published several reports on roentgen therapy in rheumatic heart disease to which the authors refer (see Absts. in Radiology **10:** 524, 1928; **13:** 282, 1929; **22:** 385, 1934) in which it was stated that the best results were obtained in patients treated during the primary attack, but this observation was not confirmed in the present series.

In a letter published in *Annals of Internal Medicine* in August 1946, Levy and Golden defend their thesis that roentgen therapy has a place in the treatment of rheumatic heart disease. In explanation of the discrepancies between their results and those of Griffith and Halley, they cite the difference in technic of irradiation and the different emphasis in the two studies. Their attention was focused upon the heart, while Griffith and Halley appear to have been chiefly concerned with the general manifestations of rheumatic fever. Levy and Golden refer to their latest paper (Am. J. M. Sc. **194:**

597, 1937. Abst. in Radiology **30:** 776, 1938), which was not mentioned by Griffith and Halley, and repeat some of the conclusions contained therein.

STEPHEN N. TAGER, M.D.

Roentgen Therapy for Rheumatic Diseases. Richard H. Freyberg. M. Clin. North America **30:** 603–615, May 1946.

Two representative cases of spondylitis rhizomélique treated by roentgen irradiation are presented. The first patient, age 21, was given three courses of irradiation, with excellent results. Five ports over the spine were used, two measuring 12 × 14 cm., one 16 × 14 cm., and two 18 × 10 cm. (a diagram is reproduced to show the location of the fields). X-ray factors were: 200 kv. (175 kv. constant potential equivalent), 0.5 mm. Cu and 1.0 mm. Al filtration, h.v.l. 0.9 mm. Cu, 50 cm. skin-target distance, and an output of 50 r (measured in air) per minute. Three ports were irradiated on the first, third, and fifth days, and two on the second, fourth, and seventh days, for a total of 600 r to each portal.

In the second case of spondylitis, the number of ports was reduced to four, but the width of the fields was increased so that more of the spinous tissue was irradiated (one field 12 × 18 cm., two 18 × 16 cm., and one 14 × 12 cm.) and a lower voltage was used. Factors were: 140 kv., 10 ma., skin-target distance 50 cm., filters 0.5 Cu and 1.0 mm. Al. Each port received 450 r (150 r × 3). This patient received two courses of irradiation. This technic was equally successful in relieving the pain and stiffness, and radiation sickness has been found to be less frequent following its use.

Thiamine hydrochloride is not given routinely during treatment but is administered if severe anorexia or nausea occurs. Pyridoxine has been found useful in relieving gastro-intestinal symptoms.

Contrary to the experience of some others, the author has found roentgen irradiation of little value in rheumatoid arthritis. Some patients with osteoarthritis obtain slight temporary relief from pain, but in most instances no subjective or objective benefit is noted. Approximately 50 per cent of patients with non-articular rheumatism were not helped.

The author concludes that roentgen irradiation should be considered as part of the therapeutic program for certain forms of arthritis but should be wisely administered, with an understanding of its limitations.

Aerotitis Media in Submariners. Henry L. Haines and J. Donald Harris. Ann. Otol., Rhin. & Laryng. **55:** 347–371, June 1946.

In order to obtain further light on the causes and effects of aerotitis media and to discover, if possible, means of prediction, prevention, and treatment, 6,149 men were submitted to 50 pounds air pressure in a submarine escape training tank. Of this number, 26.9 per cent contracted otitis media. These men were then assigned to various experimental groups to determine the effect of certain forms of therapy in preventing the development of subsequent attacks under pressure. Among the measures tried were roentgen and radium therapy. The roentgen therapy experiments, however, had to be discontinued for administrative reasons, so that no conclusions as to its effect could be reached.

For radium therapy a random sample was selected from those patients with excessive lymphoid tissue in and about the pharyngeal ostium. Fifty milligrams of radium salt was applied for eight to ten minutes. The radium was contained in a monel metal applicator 2 cm. long, with an inside diameter of 1.7 mm. and walls 0.3 mm. thick. This cylinder was brazed to a wire by which it was handled. Crowe's and Burnam's technic was followed. Successive radium treatments were given at intervals of about a month. One group was required to take a pressure test after every treatment, while another group was required to wait until a course of three to eight treatments was completed.

About 90 per cent of the 732 patients receiving radium therapy were able thereafter to sustain pressure without the development of otitis media. In at least some of the group not responding to radium therapy, the authors believe that other conditions than excess lymphoid tissue may have been the responsible factor. In one patient, for example, an old mastoiditis had caused considerable scarring, while another had a post-diphtheritic paralysis of the right side of the throat and palate. As stated above, the number of treatments varied, but it is clear from the recorded results that most ears sustained little or no damage after two applications.

Psychological therapy proved to be valueless and topical applications of a neosynephrine solution had but slight effect. Dental care in men with abnormalities of occlusion was remarkably effective.

The incidence of deafness in submarine personnel is considerably less than that reported in the Air Forces. The difference is explained in terms of the different barometric conditions which prevail between the two services. The usual flight consists of a decompression followed by return to normal pressure, while submarine training consists of a compression followed by a return to normal pressure. In the case of submariners, then, it will be seen that the negative pressure in the tympanum which produced vasuclar engorgement and rupture during the first or compression phase, changes to positive pressure during the second or decompression phase, and the result is that the vascular system tends to shrink and a form of therapy is achieved. The reverse is true for the aviators, in whom the second phase is one of compression, the men reaching the ground at a time when symptoms are most pronounced. For these reasons a greater incidence and severity of pathological changes and loss of hearing acuity might be expected among aviators than among submariners.

Another account of this study appears in U. S. Naval M. Bull. **46:** 1529, October 1946.

STEPHEN N. TAGER, M.D.

Radioactive Iodine in the Study of Thyroid Physiology. VII. Use of Radioactive Iodine Therapy in Hyperthyroidism. Saul Hertz and Arthur Roberts. J. A. M. A. **131:** 81–86, May 11, 1946.

Hertz and Roberts present their studies of the action of radioactive isotopes of iodine in 29 cases of hyperthyroidism. Two tables are included: one listing their so-called failures in 9 cases and the other giving pertinent data in 20 cases listed as cures. In 5 patients subsequently operated upon (listed as failures), hypometabolism or true myxedema developed. By excretion studies, external counter measurements over the thyroid gland, planned operations in 2 cases, and careful clinical studies, data were obtained making it possible to construct a formula for treatment procedure. Doses ranging from 5 to 25 millicuries to uniodized patients were effective in the treatment of hyperthyroid-

ism in 80 per cent of cases. The resultant dosage expressed in roentgens closely approximated the dosage of roentgen therapy in the authors' opinion. The addition of ordinary iodine therapy after administration of radioactive iodine offered many advantages in clinical care of patients and safety of the procedure. No mortalities or undesirable complications such as tetany or loss of phonation occurred. There were no undesirable radiation effects, tracheal or largyneal irritations or anemia, in any of the cases. D. A. KOCH, M.D.
(University of Michigan)

Treatment of Hyperthyroidism with Radioactive Iodine. Earle M. Chapman and Robley D. Evans. J. A. M. A. **131:** 86–91, May 11, 1946.

A report of an additional 22 carefully selected cases of hyperthyroidism treated with radioactive iodine is presented by Chapman and Evans. Their work supplements the previously reported investigations of Hertz, Roberts, and Evans. In these cases, considerably larger doses were used and no other treatment was instituted. Two tables and several B.M.R. charts as well as case histories are presented. The preparation of radioactive iodine and tissue effects are discussed. By iodine retention curves the authors were able to predict dosages and found that a patient who swallowed 14 millicuries of radioactive iodine received a radiation dose equivalent to approximately 3,490 roentgens. This radioactive iodine is carried in about one milligram or less of ordinary iodine and is concentrated largely in the thyroid gland. Reactions simulating radiation sickness were observed in 6 cases. Biopsy of the thyroid in 2 cases showed definite fibrosis following this treatment.

Cases of recurrence following surgery and patients sensitized to iodine and thiouracil responded well to this form of therapy. Recoveries were observed in 14 patients after ingestion of a single dose. Two doses were necessary in 3 patients, and in 5 patients three doses were given. Only 2 patients had signs of residual hyperthyroidism after therapy. Myxedema occurred in 4 cases. D. A. KOCH, M.D.
(University of Michigan)

DOSAGE

A Direct-Reading X-Ray Intensity Comparator. Its Radiological and Physical Applications. L. A. W. Kemp. Brit. J. Radiol. **19:** 233–242, June 1946.

The construction and calibration of a twin chamber intensity comparator is described. This may be used to measure percentage depth doses, intensity distributions across or along a beam, half-value layers, and dosage rates. SYDNEY J. HAWLEY, M.D.

Roentgen Dose Distribution in the Thorax. Experimental Study. Olof Sandström. Acta radiol. **27:** 433–439, May 6, 1946. (In German.)

The author has carried out experiments for the determination of intensity with Sievert's small condenser chamber at different depths in the lungs of newly slaughtered calves with thoracic walls of different thicknesses. The experimental appliance is described and the results are set forth graphically, the curves showing the roentgen dose at different depths as percentage of the surface dose. The results are compared with those obtained by Quimby and others in measuring the intensity in cadavers.

Radiation Measurements on a Continuously Evacuated Roentgen Tube for 400 kV. Sigvard Eklund and Sven Benner. Acta radiol. **27:** 264–268, May 6, 1946. (In English.)

Measurements of dosage rates and half-value layers of the roentgen rays from a continuously evacuated roentgen tube are reported for voltages of 250–350 kv. and for two different target designs.

EFFECTS OF RADIATION

Osteoradionecrosis of the Mandible. Edwin A. Lawrence. Am. J. Roentgenol. **55:** 733–742, June 1946.

The author believes that the pathogenesis of osteoradionecrosis is not clearly understood, probably because investigative studies with heavy protracted fractionated irradiation have not yet been reported. The three important factors in the production of the necrosis are heavy irradiation, trauma, and infection. Its occurrence in the mandible is relatively frequent following heavy irradiation for oral carcinoma.

The mandible receives its blood supply from a single nutrient artery, the inferior dental, and from the periosteum. It is formed of dense compact bone with a high calcium content. Because of this, it receives an increased amount of soft, scattered radiation resulting in a high intrinsic dose, which may exceed that of the adjacent soft tissues. It has been stated that the periosteum is highly susceptible to irradiation and that the osteoblasts may be completely destroyed, thus explaining the lack of bone regeneration after sequestrectomy or subperiosteal bone resection. The macroscopic integrity of the bone is usually maintained after exposure to heavy radiation until infection or trauma is added, following which gross disintegration of bone occurs. Apparently sound teeth in the field being irradiated may subsequently become carious, and their removal is likely to be followed by disintegration of the mandible. Prophylactically all teeth should be removed prior to irradiation. Minimally, the teeth in the direct beam should be removed and a period of at least ten days allowed before irradiation to permit healing in the tooth sockets. Rigid post-irradiation oral hygiene is important to prevent deep mucous membrane ulceration, which may eventually extend down to bone.

Once osteoradionecrosis has occurred, the lesion should be handled with extreme conservatism and no attempt made to remove the sequestrum until it has become so loose that it can be lifted out with forceps. During the long period of sequestration, the involved area should be kept as clean as possible.

Six cases illustrating the factors contributing to osteoradionecrosis, its treatment, and course are reported in detail. H. H. WRIGHT, M.D.

Treatment of Roentgen Sickness with Oral Administration of Pyridoxine Hydrochloride (Vitamin B_6). Robert J. Reeves. South. M. J. **39:** 405–407, May 1946.

One hundred cases of roentgen sickness have been ob-

served by the author since March 1944. Forty-five of these patients were being treated by roentgen rays for carcinoma of the cervix, rectum, or bladder, with an average of 8,000 to 10,000 r distributed over the pelvis. The usual field of irradiation measured 10 × 15 cm. Treatment was usually started with 150 r directed to each of two opposing ports, and this dosage was increased by 50 r daily until 300 r was being delivered to each port. Pyridoxine hydrochloride (vitamin B_6) was administered at the onset of the roentgen sickness and continued as long as nausea persisted; 50 mg. was given orally in the morning about four hours before irradiation, another 25 mg. at noon, and 25 mg. before the evening meal—a total daily dose of 100 mg. An occasional patient who did not respond to pyridoxine hydrochloride by mouth was benefited by intravenous injection. In 25 of the 45 cases in the above group, the results were good, in 16 moderate, and in 4 poor.

Among 55 patients with nausea and vomiting following roentgen irradiation over the thorax and upper abdomen for postoperative carcinoma of the breast, lymphoblastoma, polycythemia, and Marie-Strümpell arthritis, good results were obtained with pyridoxine hydrochloride in 52, moderate in 2, and poor in one.

A Clinical Syndrome Following Exposure to Atomic Bomb Explosions. Paul D. Keller. J. A. M. A. 131: 504–506, June 8, 1946.

Studies were made on 21 patients with delayed illness following exposure to atomic bomb explosions in Japan in 1945. Cases receiving severe blast injuries or extensive external burns at the time of explosion were not included. The symptoms and findings are similar to those following excessive irradiation of the body by x-rays. Within distances of 2,000 yards from the center of explosion there appeared to be no significant difference in the possibility of developing the illness. That all patients save one were indoors at the time of explosion would make it appear that delayed effects are more likely to become manifest in those who are protected, though incompletely, provided they survive the initial effects.

There were five deaths, the average interval being twenty-six days after the explosion. Patients were hospitalized after an average of one month following exposure. The delayed effects on the body are attributed to destruction or suppression of elements of the hemopoietic system (leukopenia, thrombocytopenia, increased bleeding time, hemorrhagic tendency with anemia, weakness, and fever) and disturbance of liver function (albuminuria, tyrosinuria, hypoproteinemia, jaundice, and fever). An increased erythrocyte sedimentation rate was present in evidence of extensive tissue destruction.

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Inactivation of Viruses by Radiations. D. E. Lea. Brit. J. Radiol. 19: 205–212, May 1946.

As viruses represent a position intermediate between inorganic and living tissue, their behavior under irradiation may give some light on its biological effects. The literature covering experiments on the inactivation of viruses by gamma, alpha, and x-rays is reviewed and the following conclusions are reached. Inactivation of a virus in dilute aqueous solution occurs indirectly, that is, as a secondary effect of the ionization. Larger doses are required for dry viruses or concentrated solutions, indicating that the effect under these conditions is direct. There is evidence to show that a single ionization is sufficient to inactivate a virus particle. There is a correlation between the size of the virus particle and the dose. Larger doses are required for smaller particles.

SYDNEY J. HAWLEY, M.D.

Effect of Dose Rate Variations on Mitosis and Degeneration in Tissue Cultures of Avian Fibroblasts. I. Lasnitzki. Brit. J. Radiol. 19: 250–256, June 1946.

Tissue cultures from the choroids and sclerotics of chick embryos were exposed to x-rays in varying doses and intensities. The effect of the radiation was graded by mitotic and degenerating cell counts.

At a dose of 100 r, the initial inhibition of cell division was independent of the dose rate. The rates used were 9.3, 29.8 and 101 r/m. However, mitotic recovery was slowed down and the degenerating cell counts increased with decreasing dose rates.

With doses of 2,500 r, no dividing cells were found after irradiation at 101 r/m. Attempts at mitotic recovery occurred at 29 and 9.7 r/m. At this total dosage the degenerating cells increased with increasing dose rate. Two types of degenerating cells were seen, degeneration during the resting phase and during mitosis. Mitotic degenerations were seen only after the two lower dose rates were used. A dose of 2,500 r given in two equal halves at 101 r/m, separated by an interval of five hours, was more effective than when given in one continuous dose. In this case a greater number of degenerations during mitosis were observed.

SYDNEY J. HAWLEY, M.D.

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